CHAPTER 18

Neuro-ophthalmology

Neuroimaging

Magnetic resonance imaging

Basic physics

Magnetic resonance imaging (MRI) depends on the rearrangement of hydrogen nuclei (protons—positively charged) when a tissue is exposed to a short electromagnetic pulse. When the pulse subsides, the nuclei return to their normal position, re-radiating some of the energy they have absorbed. Sensitive receivers pick up this electromagnetic echo. Unlike CT it does not subject the patient to ionizing radiation. Exposed tissues produce radiation with characteristic intensity and time patterns. The signals are analysed, computed and displayed as a cross-sectional image which may be: (a) *axial* (Fig. 18.1) (b) *coronal* (Fig. 18.2) or (c) *sagittal* (Figs 18.3, 18.4).

Relaxation times

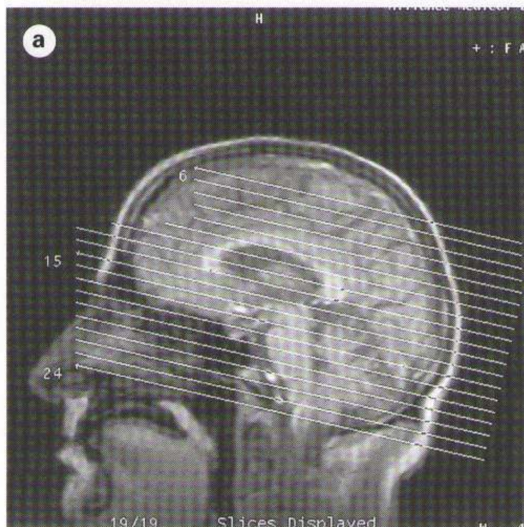
T1 and T2 weighting refers to two methods of measuring the relaxation times of the excited protons after the magnetic field has been switched off. Various body tissues have different relaxation times so that a given tissue may be T1- or T2-weighted, (i.e. best visualized on that particular type of image). In practice both types of scans are usually performed.

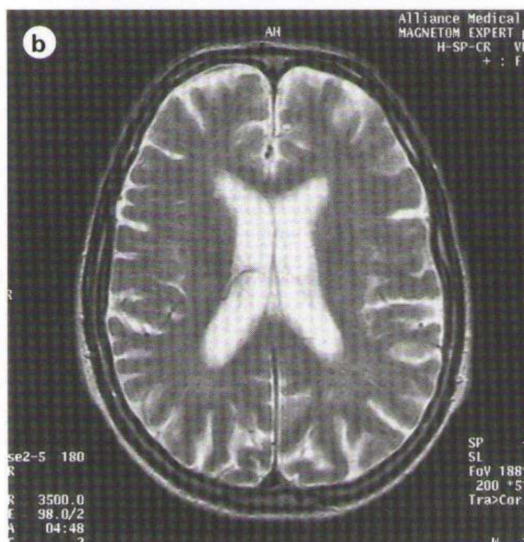
1. **T1-weighted** images are best for normal anatomy (Fig. 18.5 and *see* Fig. 18.3).
   - Hypointense (dark) structures include water and vitreous.
   - Hyperintense (bright) structures include fat and contrast agents.
2. **T2-weighted** images are usually preferred for viewing pathological changes (*see* Figs 18.1 and 18.2).
   - Hypointense structures include fat and contrast agents.
   - Hyperintense structures include vitreous and water.

> ***NB:*** Bone and calcification are invisible on MRI.

Enhancement

1. **Gadolinium** is a substance which acquires a magnetic moment when placed in an electromagnetic field.





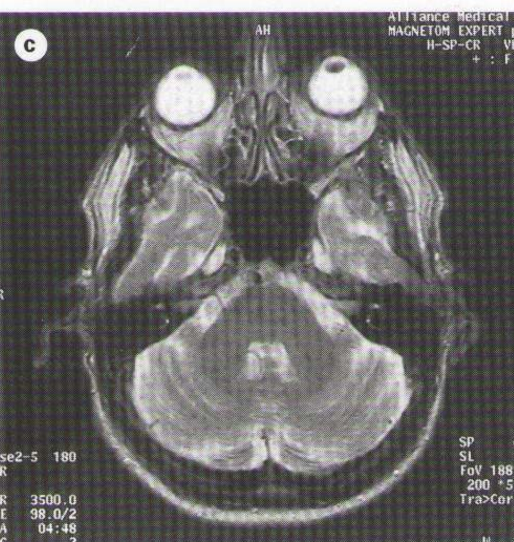


Fig. 18.1
Axial T2-weighted MRI scan

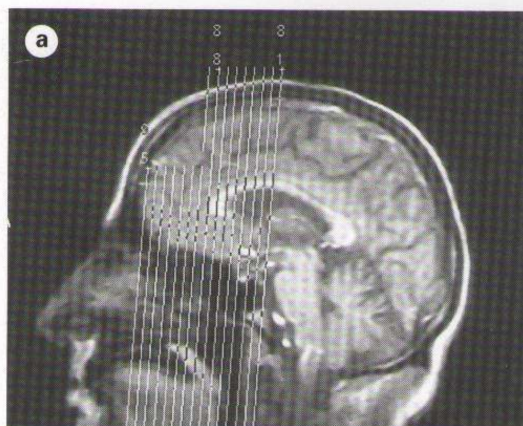
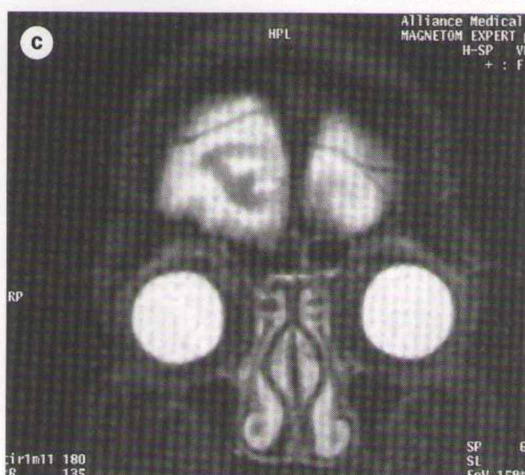


Fig. 18.2
Coronal T2-weighted MRI scan





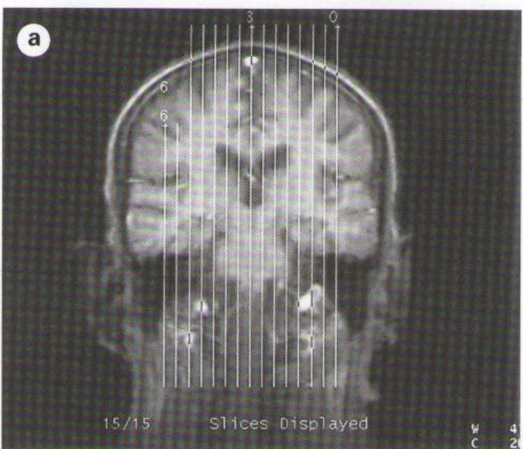
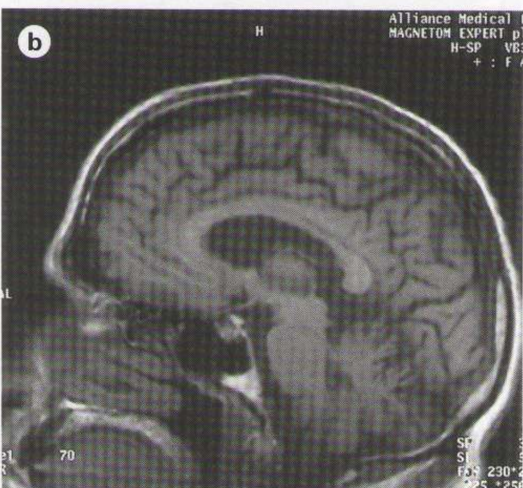
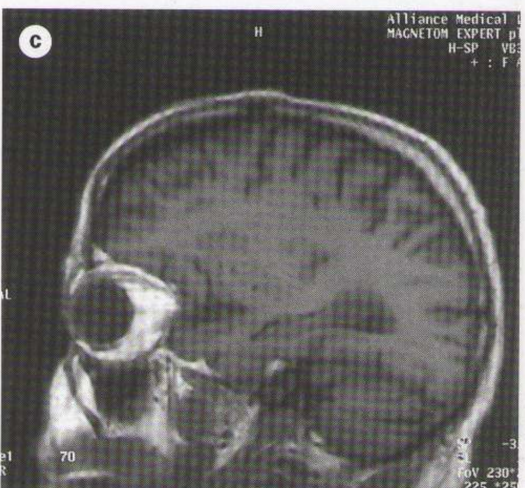


Fig. 18.3
Sagittal T1-weighted MRI scan





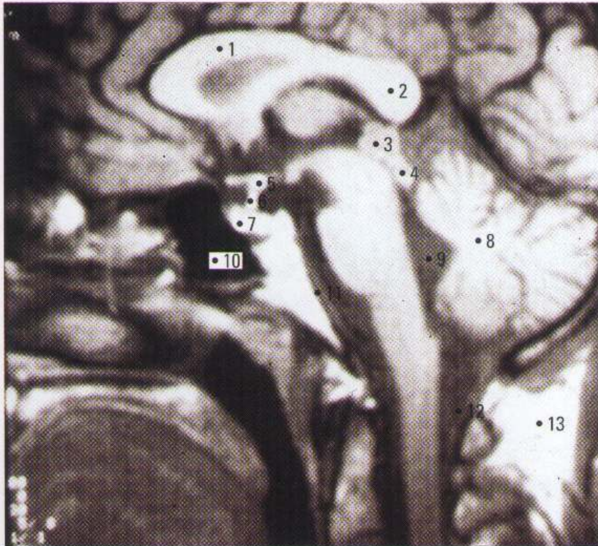


Fig. 18.4
Sagittal MRI scan showing normal anatomy. (**1**) Body of corpus callosum; (**2**) splenium of corpus callosum; (**3**) superior colliculus; (**4**) inferior colliculus; (**5**) infundibular recess; (**6**) infundibulum; (**7**) pituitary gland; (**8**) cerebellum; (**9**) fourth ventricle; (**10**) sphenoid sinus; (**11**) clivus; (**12**) foramen magnum and craniocervical junction; (**13**) subcutaneous fat
(Courtesy of K. Nischal)

Administered intravenously, it remains intravascular unless there is a breakdown of the blood–brain barrier. It is therefore extremely helpful in the detection of tumours and inflammatory lesions which appear bright on T1-weighted scans. Ideally MRI is performed both before (Fig. 18.6) and after (Fig. 18.7) administration of gadolinium. Special head or surface coils can also be used to improve spatial definition of the image. Gadolinium is safer than iodine; adverse effects are uncommon and usually relatively innocuous (e.g. nausea, hives and headache).

2. **Fat suppression** techniques are applied for imaging the orbit because the bright signal of orbital fat on conventional T1-weighted imaging frequently obscures other orbital contents. Fat suppression eliminates this bright signal and better delineates both normal structures (optic nerve and extraocular muscles) as well as tumours, inflammatory lesions and vascular malformations. The combination of gadolinium and fat suppression helps highlight areas of abnormal enhancement that might otherwise remain undetected. However, fat suppression may be associated with various artefacts and therefore should be used in conjunction with, rather than instead of, conventional imaging.

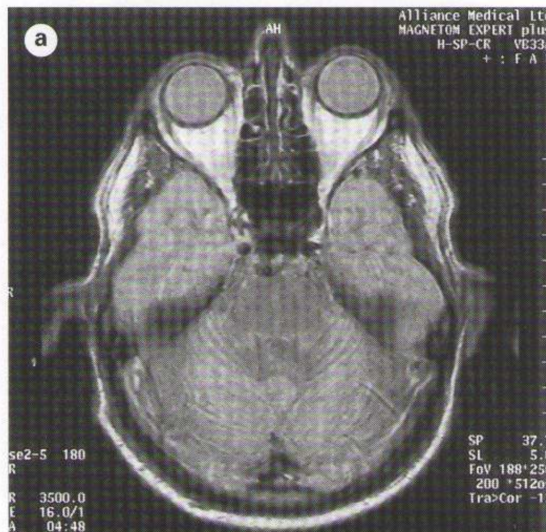
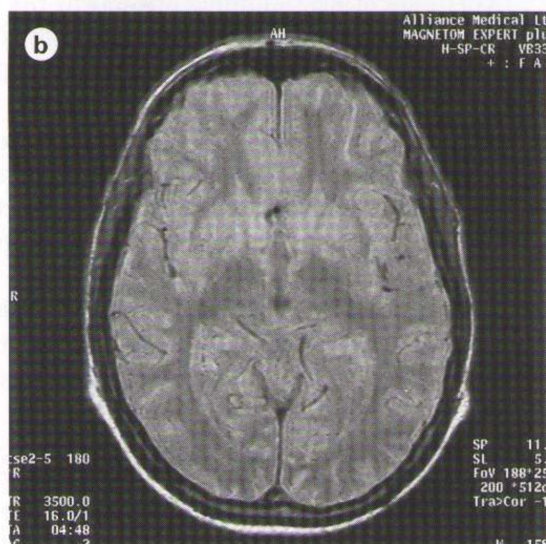


Fig. 18.5
Axial T1-weighted MRI scan



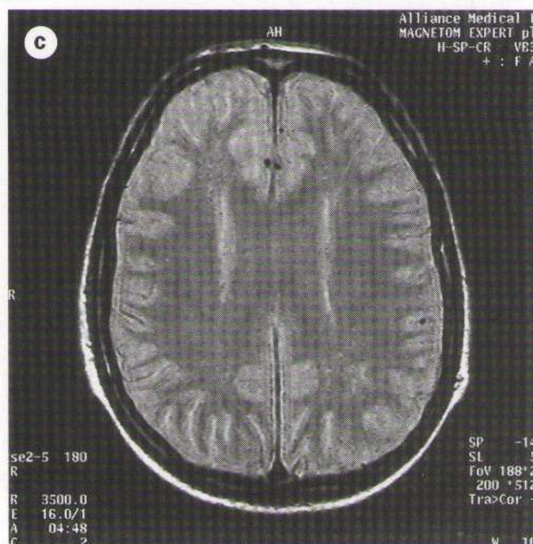




Fig. 18.6
Coronal T1-weighted unenhanced MRI scan of a pituitary adenoma (Courtesy of D. Thomas)

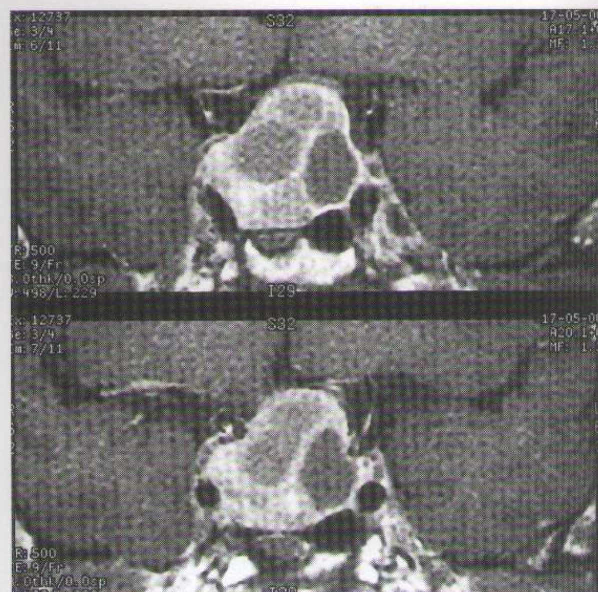


Fig. 18.7
Coronal T1-weighted gadolinium-enhanced MRI scan of a pituitary adenoma (Courtesy of D. Thomas)

Limitations of MRI

- It does not image bone (which appears black), although this is not necessarily a disadvantage.
- It does not detect recent haemorrhage and is therefore inappropriate in patients with acute intracranial bleeding.
- It cannot be used in patients with magnetic foreign objects (e.g. cardiac pacemakers, intraocular foreign bodies).
- It requires the patient to cooperate and remain motionless.
- It is difficult to perform on claustrophobic patients.

Specific neuro-ophthalmic indications

MRI is the technique of choice for lesions of the intracranial pathways. It is important to submit an accurate clinical history to the radiologist and direct attention to specific areas of potential pathology, in order to ensure appropriate imaging.

1. **The optic nerve** is best visualized by contrast-enhanced fat suppression studies using axial and coronal cuts which should include both optic nerve and the brain. MRI can detect lesions of the intraorbital part of the optic nerve (e.g. gliomas) as well as intracranial extension of orbital tumours (Fig. 18.8). In patients with retrobulbar neuritis MRI may display multiple plaques in the periventricular white matter and corpus callosum (*see* Figs 18.24 and 18.25). Since it does not image calcium MRI is not useful in detecting fractures or bony erosion.
2. **Pituitary tumours** are best visualized by contrast-enhanced studies (*see* Fig. 18.7). Coronal slices optimally demonstrate the contents of the sella turcica, while axial cuts demonstrate adjacent structures such as the carotid arteries and cavernous sinuses.
3. **Intracranial aneurysms** can often be visualized by MRI (Fig. 18.9) although intra-arterial angiography may also be required.

Magnetic resonance angiography

Magnetic resonance angiography (MRA) is a non-invasive method of imaging the intra- and extracranial carotids

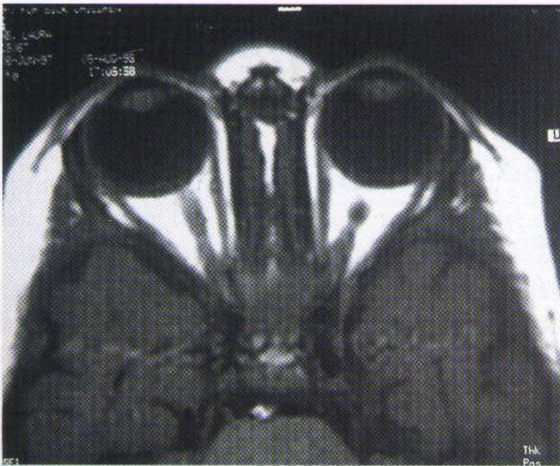


Fig. 18.8
Axial T1-weighted MRI scan showing a left optic nerve glioma involving the chiasm (Courtesy of D. Armstrong)



Fig. 18.10
MRA of the extracranial carotid circulation (Courtesy of D. Thomas)



Fig. 18.9
Axial MRI scan showing a right middle cerebral artery aneurysm (Courtesy of D. Thomas)

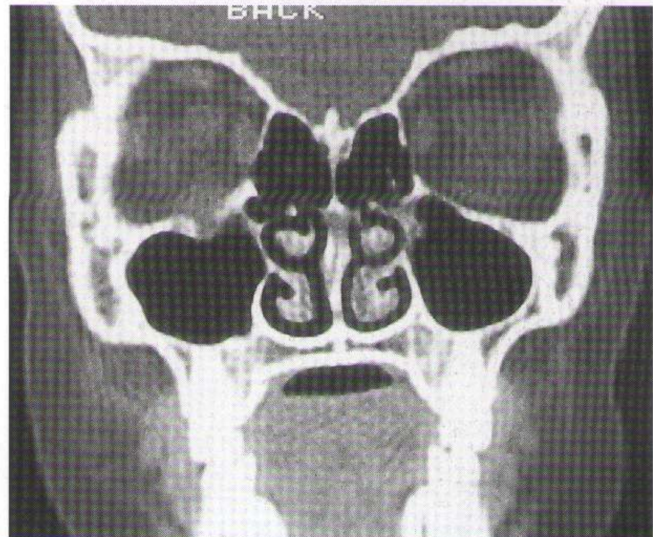


Fig. 18.11
Coronal CT scan showing a right orbital blow-out fracture

(Fig. 18.10) and vertebrobasilar circulations to demonstrate abnormalities such as stenosis, occlusion, arteriovenous malformations and aneurysms. However, MRA is not as reliable as conventional intra-arterial angiography in detecting aneurysms smaller than 5 mm in diameter. Conventional angiography therefore remains the 'gold standard' for accurate diagnosis and planning of surgery for berry aneurysms (*see* Fig. 18.110) which have caused third nerve palsies or subarachnoid haemorrhage. Even if MRA demonstrates an aneurysm, conventional angiography is ideally still required to identify additional undetected aneurysms.

Computed tomography

Computed tomography (CT) uses thin X-ray beams to obtain tissue density values from which detailed cross-sectional images are formed by a computer. The cuts may be coronal or axial but not sagittal. Lesions with intrinsic vasculature may be better visualized by iodinated contrast agents.

Clinical indications

In general, CT is easier and faster to perform than MRI but exposes the patient to ionizing radiation.

- The main advantage over MRI lies in detecting bony lesions such as fractures and erosions, and demonstrating skull anatomy. CT is therefore very useful for evaluating patients with orbital trauma and can display fractures (Fig. 18.11) and foreign bodies as well as blood, herniation of extraocular muscles and emphysema.
- CT can also detect intraocular calcification (optic disc drusen and retinoblastoma).
- CT is preferable for acute cerebral (Fig. 18.12) or subarachnoid haemorrhage because the lesions may not appear on MRI for hours.
- CT is as good or superior to MRI with fat suppression in demonstrating enlarged extraocular muscles in thyroid eye disease (*see* Fig. 17.16).
- CT can be used when MRI is contraindicated (i.e. patients with ferrous foreign bodies).



Fig. 18.12
Axial CT scan showing acute intracerebral haemorrhages
(Courtesy of L. Webb)

Optic nerve

Applied anatomy

General structure

1. **Afferent fibres.** The optic nerve carries about 1.2 million afferent nerve fibres, which originate in the retinal ganglion cells. Most of these synapse in the lateral geniculate body, although some reach other centres, notably the pre-tectal nuclei in the midbrain. Nearly one-third of the fibres subserve the central 5° of the visual field. Within the optic nerve itself the nerve fibres are divided into about 600 bundles (each containing 2000 fibres) by fibrous septa derived from the pia mater (Fig. 18.13).
2. **Oligodendrocytes** provide axonal myelination. Congenital myelination of retinal nerve fibres is the result of anomalous intraocular extension of these cells.
3. **Microglia** are immunocompetent phagocytic cells which probably modulate apoptosis (programmed death) of retinal ganglion cells.
4. **Astrocytes** line the spaces between axons and other structures. When axons are lost in optic atrophy astrocytes fill in the empty spaces.
5. **Surrounding sheaths**
   a. ***Pia mater*** is the delicate innermost sheath containing blood vessels.
   b. ***Subarachnoid space*** is continuous with the cerebral subarachnoid space and contains cerebrospinal fluid (CSF).
   c. ***Outer sheath*** comprises the arachnoid mater and the tougher dura mater. The latter is continuous with the sclera. Optic nerve fenestration involves incision of the outer sheath.

Anatomical subdivisions

The optic nerve is approximately 50 mm long from globe to chiasm and can be subdivided into four segments:

1. **Intraocular** segment (optic disc, nerve head) is the shortest, being 1 mm deep and 1.5 mm in vertical diameter. Neurological disorders affecting this part of the optic nerve include inflammation (papillitis), oedema and abnormal deposits (drusen). In relation to the lamina cribrosa the intraocular segment can be further subdivided into three zones:
   - The prelaminar zone is supplied by very small branches of the central retinal artery.
   - The laminar and postlaminar zones are supplied by branches of the short posterior ciliary arteries via the anastomotic circle of Zinn (which also receives input

from the parapapillary choroid and pial arterial network).

2. **Intraorbital** segment is 25–30 mm long and extends from the globe to the optic foramen at the orbital apex. Its diameter is 3–4 mm because of the addition of the myelin sheaths to the nerve fibres. At the orbital apex the nerve is surrounded by the tough fibrous annulus of Zinn, from which originate the four rectus muscles. Because the superior and medial rectus muscles partly originate from the nerve sheath itself, inflammatory optic neuropathy (e.g. retrobulbar neuritis) may be associated with pain on ocular movement. Within the orbit the optic nerve is slack and S-shaped, allowing for eye movements without stretching.

> *NB:* Because of this redundancy the optic nerve does not become unduly stretched until proptosis is severe.

3. **Intracanalicular** segment traverses the optic canal and measures about 6 mm. Unlike the intraorbital portion it is fixed to the canal, since the dura mater fuses with the periosteum.
4. **Intracranial** segment joins the chiasm and varies in length from 5 to 16 mm (average 10 mm). Long intracranial segments are particularly vulnerable to damage by adjacent lesions such as pituitary adenomas and aneurysms.

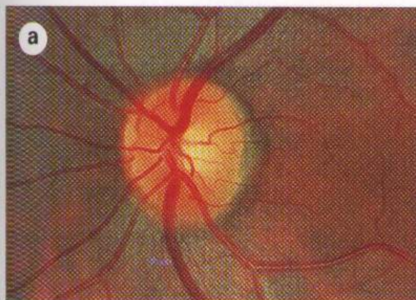
Axoplasmic transport

Axoplasmic transport is the movement of cytoplasmic organelles within a neurone between the cell body and the terminal synapse (Fig. 18.14a and b). Orthograde transport involves movement from cell body to synapse and retrograde transport is characterized by the converse. Rapid axoplasmic transport is an active mechanism requiring oxygen and is energized by ATP. Axoplasmic flow may be interrupted by a variety of insults including hypoxia and toxins which interfere with ATP production. Retinal cotton wool spots are the result of accumulation of organelles due to interruption of axoplasmic flow between the retinal ganglion cells and their terminal synapses. Papilloedema is similarly caused by hold-up of axoplasmic flow at the lamina cribrosa (Fig. 18.14c and d).

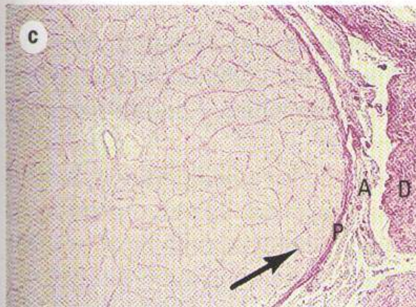
Evaluation of optic nerve disease

Signs of optic nerve dysfunction

1. **Reduced visual acuity** for distance and near is common (but may also occur with a great variety of other disorders).
2. **Afferent pupillary defect** (*see* later).







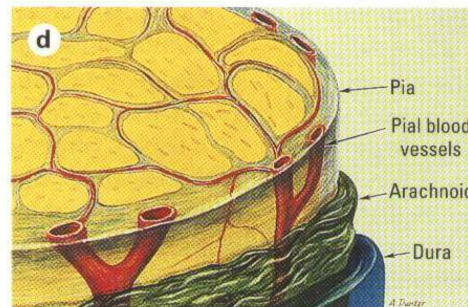


Fig. 18.13
Structure of the optic nerve. (**a**) Clinical appearance; (**b**) longitudinal section, LC = lamina cribrosa, arrow points to a fibrous septum; (**c**) transverse section, P = pia; A = arachnoid; D = dura; (**d**) surrounding sheaths and pial blood vessels (Courtesy of Wilmer Institute)

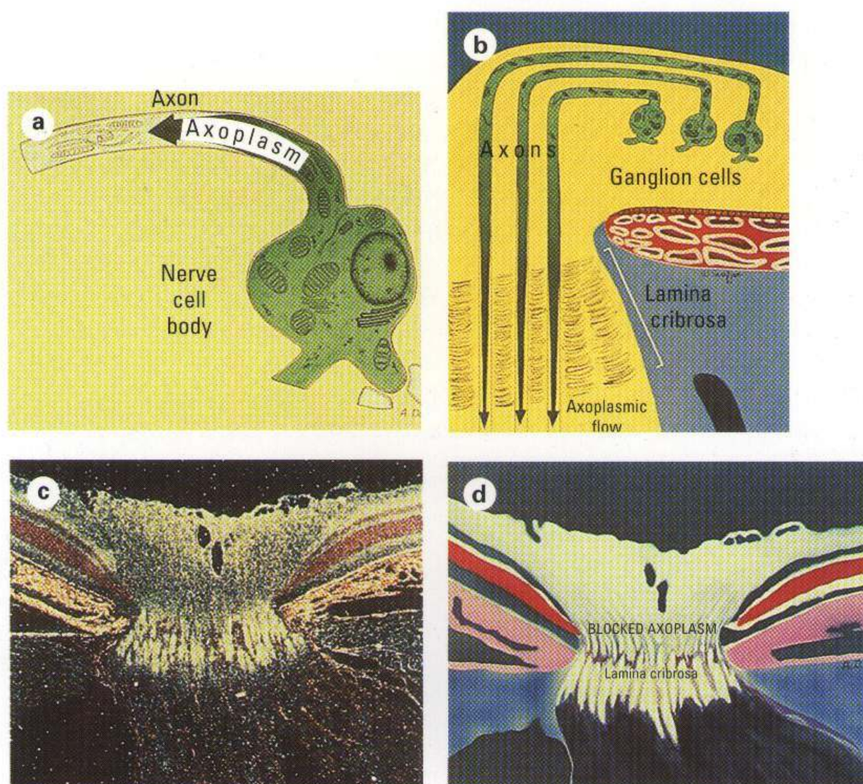


Fig. 18.14
(**a** and **b**) Axoplasmic flow; (**c** and **d**) interrupted axoplasmic flow at the lamina cribrosa in papilloedema (Courtesy of Wilmer Institute)

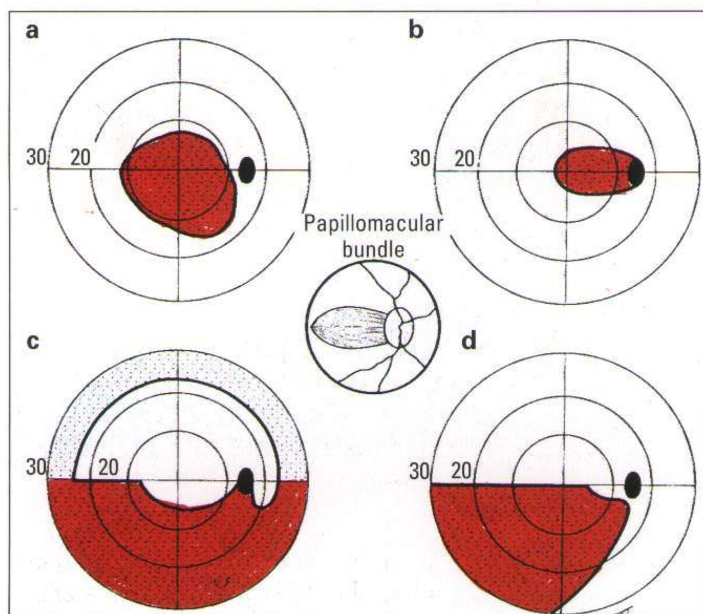


Fig. 18.15
Visual field defects in optic nerve disease. (**a**) Central scotoma; (**b**) centrocaecal scotoma; (**c**) nerve fibre bundle; (**d**) altitudinal

3. **Dyschromatopsia** (impairment of colour vision), which mainly affects red and green. A simple way of detecting a uniocular colour vision defect is to ask the patient to compare the colour of a red object between the two eyes. More accurate assessment requires the use of Ishihara pseudo-isochromatic plates, a City University chart or the Farnsworth–Munsell 100-hue test (*see* Chapter 13).
4. **Diminished light brightness sensitivity**, which may persist after visual acuity returns to normal (as seen after a previous attack of optic neuritis). This is best demonstrated as follows:
   a. A light from an indirect ophthalmoscope is shone first into the normal eye and then into the eye with the suspected optic nerve lesion.
   b. The patient is asked whether the light is symmetrically bright in both eyes.
   c. The patient will report that the light appears less bright in the affected eye.
   d. The patient is requested to assign a relative value to the brightness of the light in the diseased eye, as compared with the normal eye.
5. **Diminished contrast sensitivity**, which is tested by asking the patient to identify gratings of gradually increasing contrast, over a range of spatial frequencies (the Arden plates). This is very sensitive to subtle visual loss, although it is not specific to optic nerve disease. Contrast sensitivity may also be estimated with the Pelli–Robson chart, in which letters of gradually diminishing contrast (arranged in triplets) are read.
6. **Visual field defects**, which vary with the underlying pathology, include diffuse depression of the central visual field, central scotomas, centrocaecal scotomas, nerve fibre bundle and altitudinal (Fig. 18.15).

Optic disc changes

There is no direct correlation between the appearance of the optic disc and visual function. The four main appearances in acquired optic nerve disorders are the following:

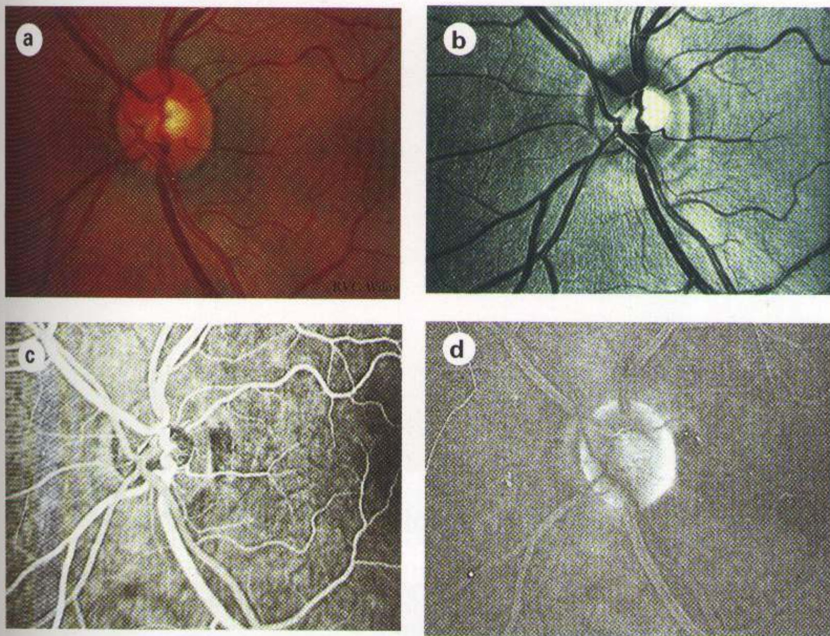


Fig. 18.16
Normal optic disc. (**a**) Clinical appearance; (**b**) red-free photography showing retinal nerve fibre striations; (**c**) venous phase FA; (**d**) late phase FA showing slight hyperfluorescence of the disc due to staining (Courtesy of Wilmer Institute)

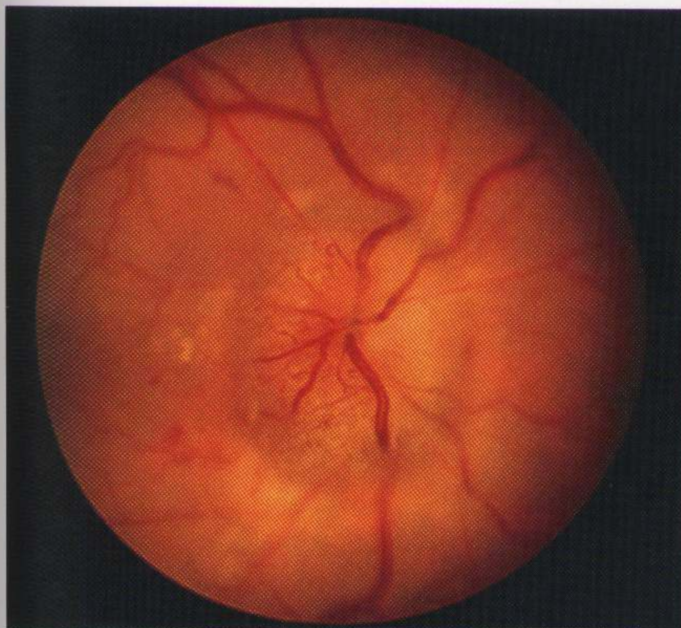


Fig. 18.17
Disc swelling due to papilloedema

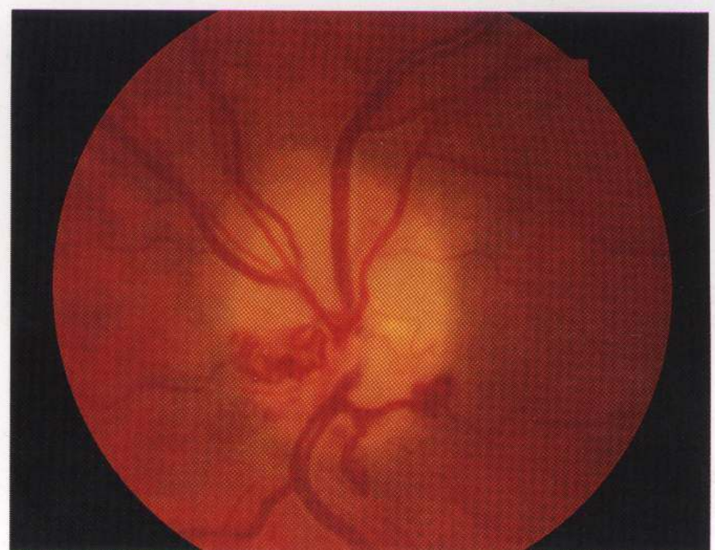


Fig. 18.18
Opticociliary shunts

1. **Normal disc** (Fig. 18.16) is classically associated with retrobulbar neuritis, although the disc may initially appear normal in Leber optic neuropathy and compressive lesions.
2. **Disc swelling** (Fig. 18.17) is a feature of papilloedema, anterior ischaemic optic neuropathy, papillitis and the acute stage of Leber optic neuropathy. It may also occur with compressive lesions before the development of optic atrophy.
3. **Opticociliary shunts** (Fig. 18.18) represent retino-choroidal venous collaterals at the optic disc, and develop as a compensatory mechanism for chronic venous compression most frequently caused by optic nerve sheath meningioma and occasionally optic nerve glioma.
4. **Optic atrophy**, which represents the end result of almost any of the aforementioned clinical conditions (*see* later).

Special investigations

1. **Manual kinetic perimetry** (Goldmann) is useful in the evaluation of neuro-ophthalmological disease, since it affords assessment of the peripheral field.
2. **Automated perimetry** quantitates the threshold retinal sensitivity to a static target. The most useful strategy tests the central 30° with points straddling the midline (e.g. Humphrey 30-2).
3. **MRI** is the method of choice for imaging the optic nerves. The orbital segment of the optic nerve is best demonstrated by fat suppression techniques by which the bright signal from orbital fat in T1-weighted images is eliminated.

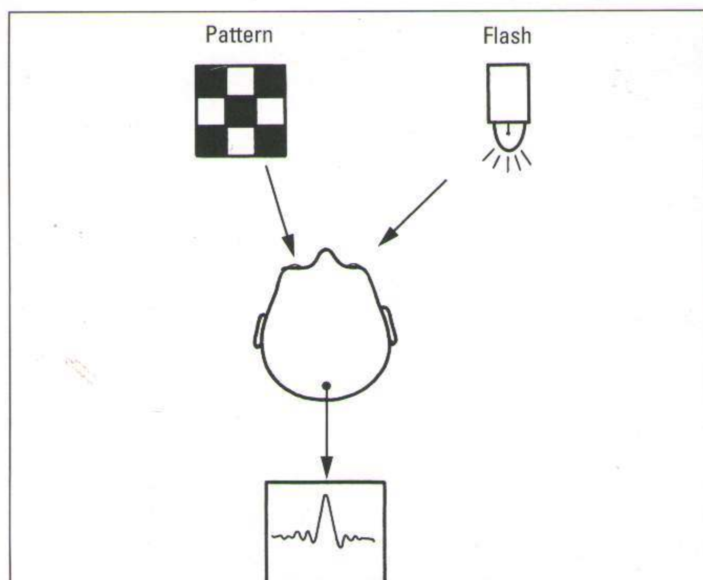


Fig. 18.19
Principles of visually evoked potential

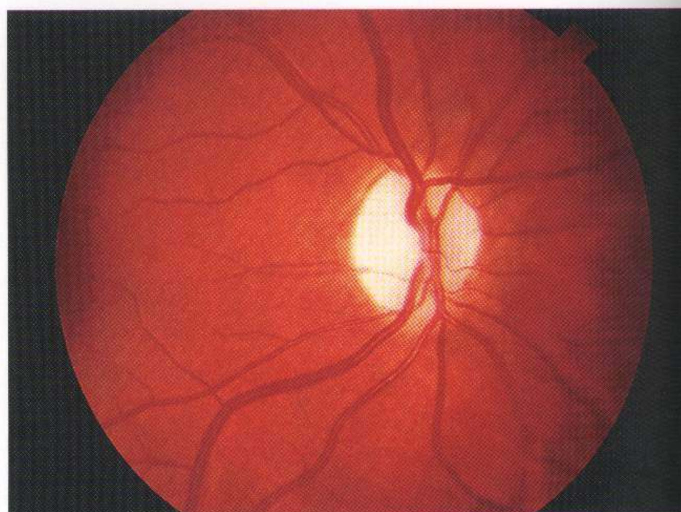


Fig. 18.20
Primary optic atrophy

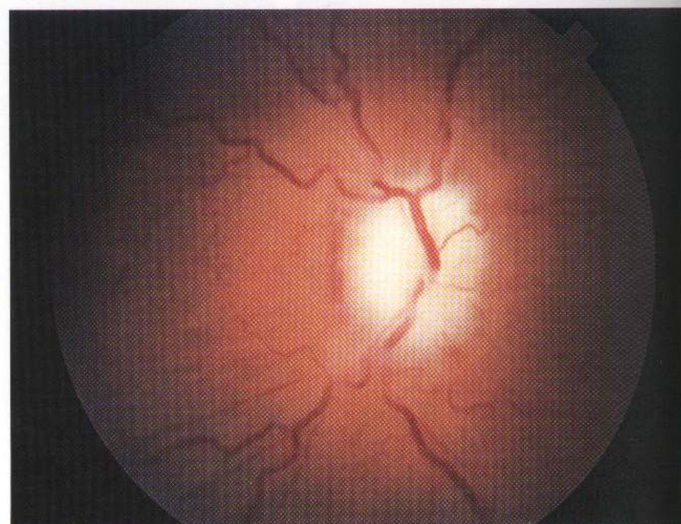


Fig. 18.21
Secondary optic atrophy

The intracanalicular and intracranial segments are better visualized on MRI than CT because of the absence of bony artefacts with the former.

4. **Visually evoked potential** (VEP) is a recording of electrical activity of the visual cortex created by stimulation of the retina. The stimulus is either a flash of light (flash VEP) or a black-and-white checker-board pattern, which periodically reverses polarity on a screen (pattern VEP) (Fig. 18.19). Several tests are performed and the average potential is calculated by a computer. Both latency (delay) and amplitude of the VEP are assessed. In optic neuropathy both parameters are affected, with prolongation of latency and decrease in amplitude of the VEP.
5. **Fluorescein angiography** (FA) may occasionally be helpful in the differentiation of papilloedema, in which there is disc leakage (*see* Fig. 18.50), from optic disc drusen, which do not leak, but auto-fluoresce (*see* Fig. 18.48).

Optic atrophy

Optic atrophy, an important sign of advanced optic nerve disease, may be primary or secondary.

Primary optic atrophy

This occurs without antecedent swelling of the optic nerve head. It may be caused by lesions affecting the visual pathways from the retrolaminar portion of the optic nerve to the lateral geniculate body. Lesions anterior to the optic chiasm result in unilateral optic atrophy, whereas those involving the chiasm and optic tract will cause bilateral optic atrophy.

1. **Causes**
   - Following retrobulbar neuritis.
   - Compressive lesions such as tumours and aneurysms (this may also result in secondary atrophy).
   - Hereditary optic neuropathies.
   - Toxic and nutritional optic neuropathies.
2. **Signs** (Fig. 18.20)
   - Pale, flat disc with clearly delineated margins.
   - Reduction in number of small blood vessels on the disc surface (Kestenbaum sign).
   - Attenuation of parapapillary blood vessels and thinning of the retinal nerve fibre layer.
   - The atrophy may be diffuse or sectoral depending on the cause and level of the lesion. For example, optic atrophy caused by chiasmal lesions may involve the nasal and temporal portions of the disc, but spare the superior and inferior (bow-tie atrophy) (*see* Fig. 18.106).

NB: Temporal pallor, however, may indicate atrophy of fibres from the papillo-macular bundle, which enter the optic nerve head on the temporal side.

Secondary optic atrophy

Secondary optic atrophy is preceded by swelling of the optic nerve head.

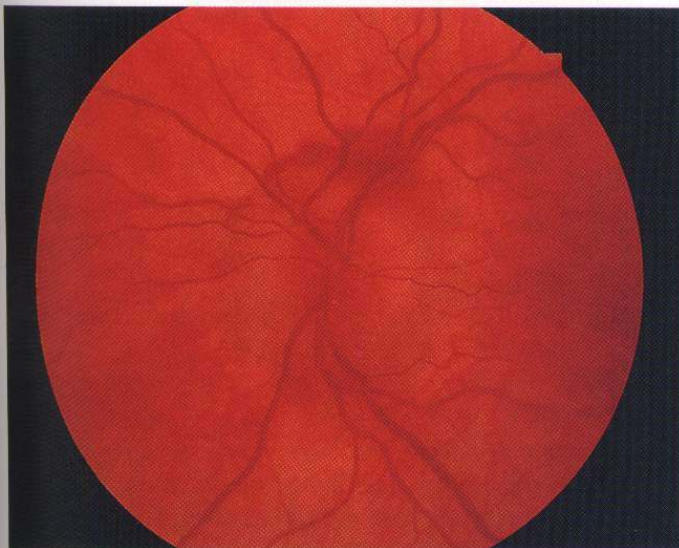
1. **Causes** include chronic papilloedema, anterior ischaemic optic neuropathy and papillitis.
2. **Signs** vary according to the cause. The main features are (Fig. 18.21):
   - White or dirty grey, slightly raised disc with poorly delineated margins due to gliosis.
   - Reduction in number of small blood vessels on the disc surface.

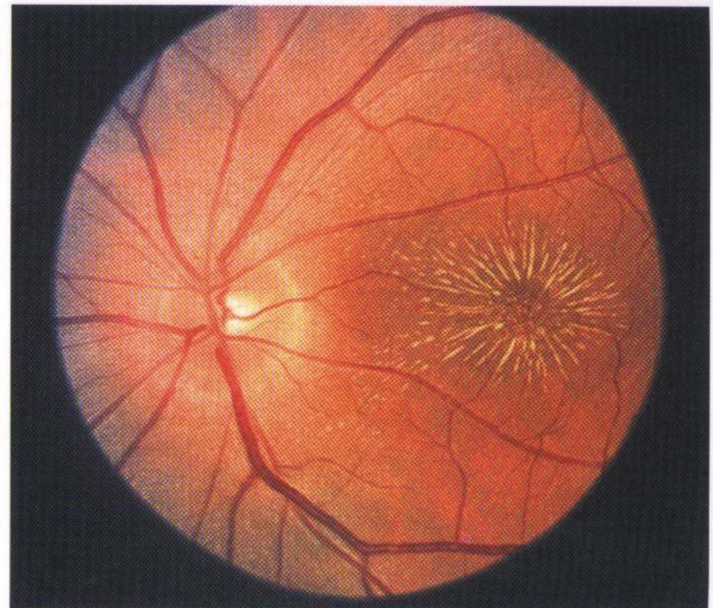
Optic neuritis

Optic neuritis is an inflammatory, infective or demyelinating process affecting the optic nerve. It can be classified both ophthalmoscopically and aetiologically as follows.

Ophthalmoscopic classification

1. **Retrobulbar neuritis**, in which the optic disc appearance is normal, at least initially, because the optic nerve head is not involved. It is the most frequent type in adults and is frequently associated with multiple sclerosis (MS).
2. **Papillitis**, in which the pathological process affects the optic nerve head primarily, or secondary to contiguous retinal inflammation. It is characterized by variable hyperaemia and oedema of the optic disc, which may be associated with parapapillary flame-shaped haemorrhages (Fig. 18.22). Cells in the posterior vitreous may be seen. Papillitis is the most common type of optic neuritis in children, although it can also affect adults.
3. **Neuroretinitis** is characterized by papillitis in association with inflammation of the retinal nerve fibre layer. A macular star figure composed of hard exudates may not be present initially, but becomes apparent within a few days or weeks and tends to become more prominent as the optic disc swelling is resolving (Fig. 18.23). In some cases there is associated parapapillary retinal oedema and serous elevation of the macula. Neuroretinitis is the least common type of optic neuritis and is most frequently associated with viral infections and cat-scratch fever. Other causes include syphilis and Lyme disease. In most cases it is a self-limiting disorder which resolves within 6–12 months.


Fig. 18.22
Papillitis


Fig. 18.23
Neuroretinitis

> ***NB:*** Neuroretinitis is never a manifestation of demyelination.

Aetiological classification

1. **Demyelinating**, which is by far the most common cause.
2. **Parainfectious**, which may follow a viral infection or immunization.
3. **Infectious**, which may be sinus-related, or associated with cat-scratch fever, syphilis, Lyme disease, cryptococcal meningitis in patients with AIDS and herpes zoster.
4. **Autoimmune**, which may be associated with systemic autoimmune diseases.

Demyelination

Demyelination is a pathological process by which normally myelinated nerve fibres lose their insulating myelin layer. The myelin is phagocytosed by microglia and macrophages, subsequent to which astrocytes lay down fibrous tissue (the plaque). A demyelinating disease disrupts nervous conduction within the white matter tracts within the brain, brain stem and spinal cord; peripheral nerves are not involved.

1. **Demyelinating diseases** which may cause ocular problems are the following:
   a. ***Isolated optic neuritis***, with no clinical evidence of generalized demyelination, although in a high proportion of cases this subsequently develops.
   b. ***Multiple sclerosis*** (MS), which is by far the most common (*see* Chapter 20).

c. Devic disease (neuromyelitis optica), which is a rare disease that may occur at any age. It is characterized by bilateral optic neuritis and subsequent development of transverse myelitis (demyelination of the spinal cord) within days or weeks.

d. Schilder disease, which is a very rare, relentlessly progressive, generalized disease with an onset prior to the age of 10 years and death within 1–2 years. Bilateral optic neuritis without subsequent improvement may occur.

2. Ocular features

a. Visual pathway lesions most frequently involve the optic nerves and cause optic neuritis. Demyelination may occasionally involve the optic chiasm, and rarely the optic tracts or radiations.

b. Brain stem lesions may result in internuclear ophthalmoplegia and gaze palsies, ocular motor cranial nerve palsies, trigeminal and facial nerve palsies and nystagmus.

3. Association of optic neuritis with MS. Although some patients with optic neuritis have no clinically demonstrable associated systemic disease, the following close association exists between optic neuritis and MS.



Fig. 18.24
Sagittal T1-weighted MRI scan showing periventricular plaques of demyelination



Fig. 18.25
Axial T2-weighted MRI scan showing periventricular plaques of demyelination

- Patients who develop optic neuritis but have a normal brain MRI have a 16% probability of developing MS within 5 years.
- At the first episode of optic neuritis, approximately 50% of patients with no other signs of MS will show demyelinating lesions on MRI (Figs 18.24 and 18.25). These patients carry a high risk of developing clinical MS within 5–10 years.
- Evidence of optic neuritis may be found in 70% of established MS cases.
- In a patient with optic neuritis the subsequent risk of MS is increased with winter onset, HLA-DR2 positivity and Uhtoff phenomenon (worsening of symptoms on elevation of body temperature, such as with exercise or a hot bath).

Demyelinating optic neuritis

1. Presentation is with subacute monocular visual impairment; rarely both eyes are involved simultaneously. Discomfort in or around the eye is common and frequently exacerbated by ocular movements. The discomfort may precede or accompany the visual loss and usually lasts a few days. Frontal headache and tenderness of the globe are present in some patients.

2. Signs

- Visual acuity is usually between 6/18 and 6/60 although rarely it may be reduced to no light perception.
- The optic disc is normal in the majority of cases (retrobulbar neuritis); the remainder show papillitis.
- Temporal disc pallor may be seen in the fellow eye, indicative of previous optic neuritis.
- Dyschromatopsia is universal and frequently worse than would be expected for that level of visual impairment.
- Other features of optic nerve dysfunction are present, as previously described.

3. Visual field defects

- The most common is diffuse depression of sensitivity in the entire central 30°, followed in frequency by altitudinal/arcuate defects and then by focal central/centrocaecal scotomas.
- Focal defects are frequently accompanied by an element of superimposed generalized depression.
- The asymptomatic fellow eye may also manifest visual field loss at presentation.

4. Course. Recovery typically begins within 2–3 weeks and continues over a period of 6 months, when maximal recovery is reached.

5. Prognosis. Approximately 75% of patients recover visual acuity to 6/9 or better; 85% recover to 6/12 or better, even if visual acuity was reduced to no light perception during the attack. However, despite return of visual acuity other parameters of visual function, such as colour vision, contrast sensitivity and light brightness appreciation, often remain abnormal. A mild afferent pupillary defect may persist and optic atrophy may ensue, particularly following recurrent attacks.

6. Treatment

a. Indications

- When the presenting visual loss is mild, treatment is probably unnecessary.
- When visual acuity within the first week of onset is worse than 6/12, treatment may speed up recovery by several weeks. This is relevant in the context of bilateral acute involvement, which is uncommon, or those who have poor vision in the fellow eye.

b. Regimen

- Intravenous methylprednisolone sodium succinate (1 g daily) for 3 days followed by oral prednisolone (1 mg/kg daily) for 11 days.

c. Benefits

- Delays further neurological events consistent with MS by 2 years.
- Hastens visual recovery from optic neuritis but does not appear to have any long-term benefit on final visual acuity.

NB: Oral steroids alone are contraindicated because they offer no benefit and double the recurrence rate of optic neuritis. Intramuscular interferon beta-1a at the time of the first episode of optic neuritis is beneficial in reducing the development of clinical demyelination in patients at high risk of MS based on the presence of subclinical brain MRI lesions.

Parainfectious optic neuritis

Optic neuritis may be associated with various viral infections such as measles, mumps, chickenpox, rubella, whooping cough and glandular fever. It may also occur following immunization. Children are affected much more frequently than adults.

1. **Presentation** is usually 1–3 weeks following a viral infection with acute severe visual loss, which may involve both eyes. This may be associated with other neurological features such as headache, seizures or ataxia (meningo-encephalitis).
2. **Signs**. The optic discs most frequently manifest bilateral papillitis although occasionally there may be a neuro-retinitis or the discs may be normal.
3. **Treatment** is not required in the vast majority of patients because the prognosis for spontaneous visual recovery is very good. However, when visual loss is severe and bilateral or involves an only seeing eye, intravenous steroids should be considered.

Infectious optic neuritis

1. **Sinus-related** optic neuritis is an infrequent condition characterized by recurrent attacks of unilateral visual loss associated with severe headache and spheno-ethmoidal sinusitis. Possible mechanisms of optic neuropathy include direct spread of infection, occlusive vasculitis and bony defects in the wall of the sinus. Treatment is with systemic antibiotics and, if appropriate, surgical drainage.
2. **Cat-scratch fever** (benign lymphoreticulosis) is a self-limiting systemic infection characterized by regional lymphadenopathy preceded by a cat-scratch (*see* Chapter 20). The organism is susceptible to doxycycline, rifampicin, ciprofloxacin and co-trimoxazole. The prognosis is excellent, with recovery of vision within 1–4 weeks of starting therapy.
3. **Syphilis** may cause acute papillitis or neuroretinitis during the primary or secondary stages (*see* Chapter 20). Involvement may be unilateral or bilateral and is frequently associated with a mild vitritis.
4. **Lyme disease** (borreliosis) is a spirochaetal infection transmitted by a tick bite. It may cause neuroretinitis and occasionally acute retrobulbar neuritis, associated with other neurological manifestations, which may mimic MS (*see* Chapter 20). Treatment of neurological involvement is with intravenous ceftriaxone 2 g daily for 14 days.
5. **Cryptococcal** meningitis in patients with AIDS may be associated with acute optic neuritis, which may be bilateral.
6. **Varicella zoster virus** most frequently causes papillitis by spread from contiguous retinitis (i.e. acute retinal necrosis, progressive outer retinal necrosis). Primary optic neuritis is uncommon but may occur in immuno-compromised patients, some of whom may subsequently develop viral retinitis. Treatment is with intravenous antiviral agents.

Non-arteritic anterior ischaemic optic neuropathy

Pathogenesis

Non-arteritic anterior ischaemic optic neuropathy (NAION) is a partial or total infarction of the optic nerve head caused by occlusion of the short posterior ciliary arteries. It typically occurs as an isolated event in patients between the ages of 45 and 65 years with structural crowding of the optic nerve head so that the physiological cup is either very small or absent. Predisposing systemic conditions include hypertension, diabetes mellitus, hypercholesterolaemia, collagen vascular disease, antiphospholipid antibody syndrome, sudden hypotensive events and cataract surgery.

Clinical features

1. **Presentation** is with sudden, painless, monocular visual loss which is not associated with premonitory visual obscurations. Visual loss is frequently discovered on awakening, suggesting that nocturnal hypotension may play an important role.
2. **Signs**

   a. Visual acuity, in about 30% of patients, is normal or only slightly reduced. The remainder have moderate to severe impairment.

b. ***Visual field defects*** are typically inferior altitudinal but central, paracentral, quadrantic and arcuate defects may also be seen.
c. ***Dyschromatopsia*** is proportional to the level of visual impairment in contrast to optic neuritis in which colour vision may be severely impaired when visual acuity is reasonably good.
d. ***Disc*** is pale with diffuse or sectoral oedema which may be surrounded by a few splinter-shaped haemorrhages (Fig. 18.26a). The oedema gradually resolves and pallor ensues (Fig. 18.27a).

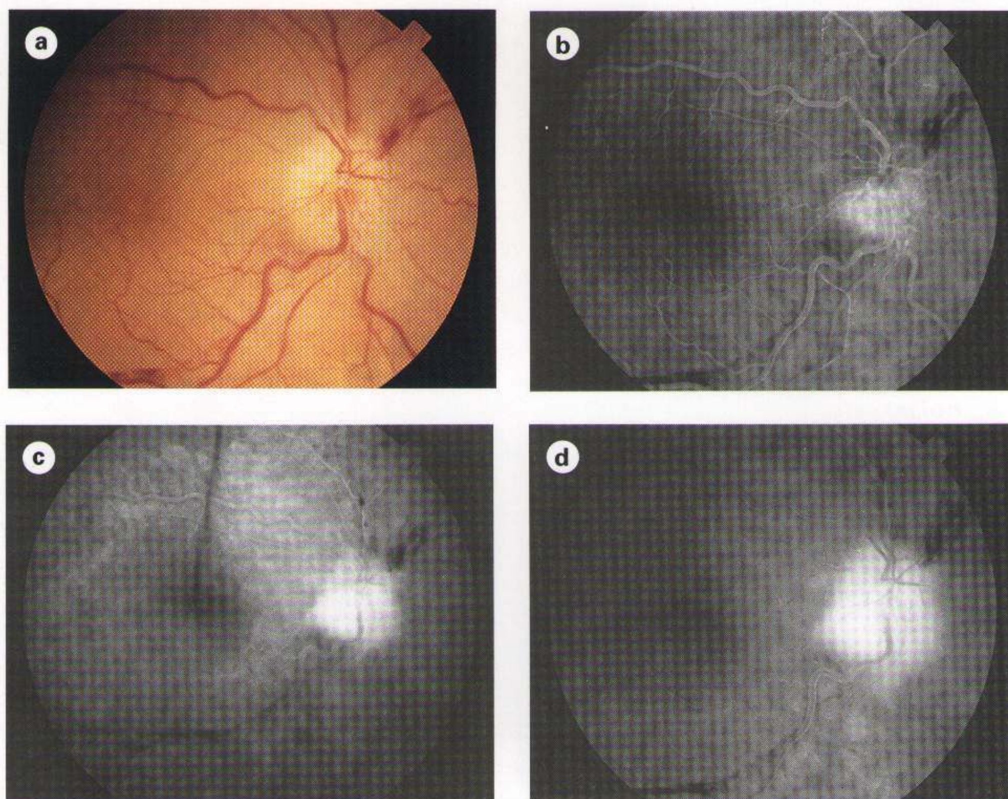


Fig. 18.26
Acute non-arteritic anterior ischaemic optic neuropathy (*see text*) (Courtesy of S. Milewski)

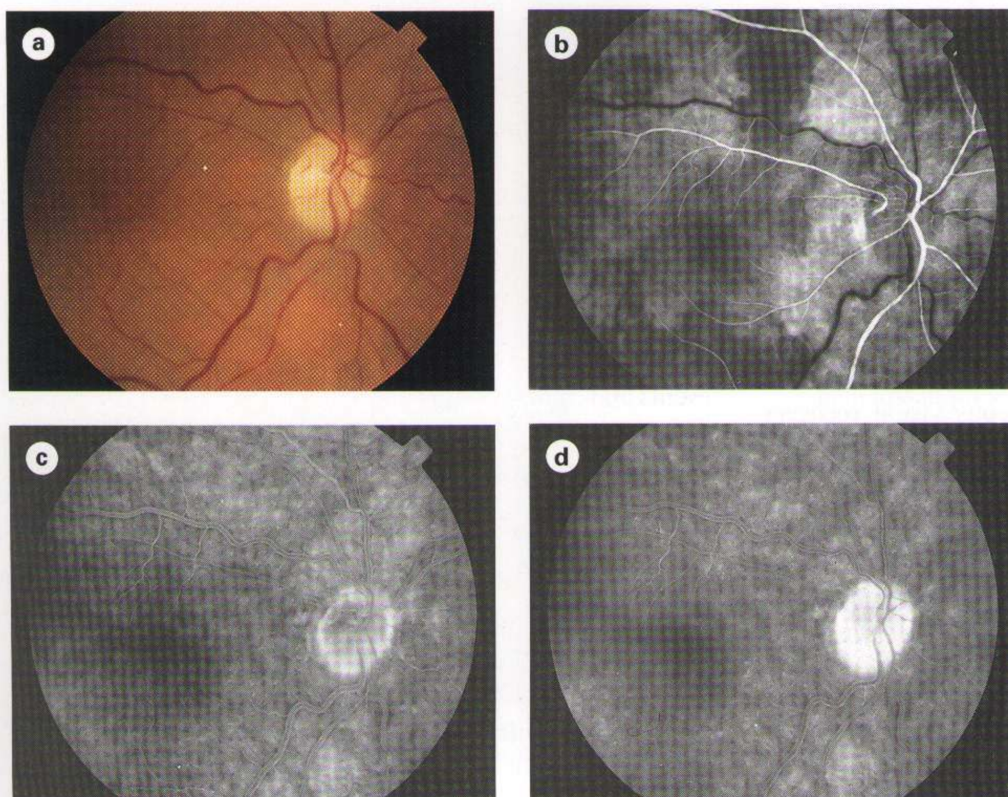
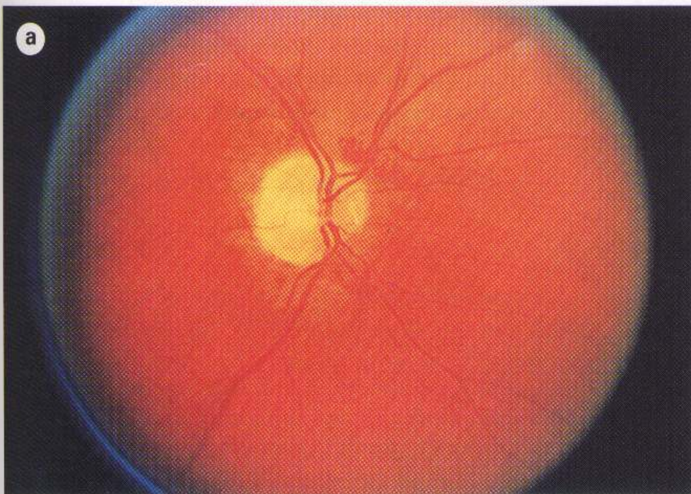


Fig. 18.27
Optic atrophy following non-arteritic anterior ischaemic optic neuropathy (*see text*) (Courtesy of S. Milewski)



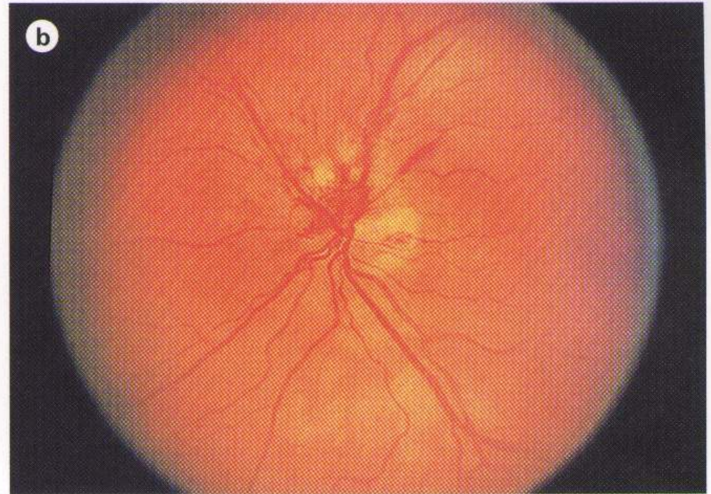


Fig. 18.28
Pseudo-Foster Kennedy syndrome associated with non-arteritic anterior ischaemic optic neuropathy (*see* text) (Courtesy of Wilmer Institute)

3. **FA** during the acute stage shows localized disc hyperfluorescence (Fig. 18.26b) which becomes more intense and then eventually involves the entire disc (Fig. 18.26c and d). Once optic atrophy develops, FA shows unequal choroidal filling during the arterial phase (Fig. 18.27b); the late stages show increasing disc hyperfluorescence (Fig. 18.27c and d).
4. **Special investigations** include serological studies, fasting lipid profile and blood glucose. It is also very important to exclude occult giant cell arteritis and other autoimmune diseases.

Prognosis

There is no definitive treatment although any underlying systemic predispositions should be treated and smoking discouraged. In most patients there is no further loss of vision although, in a small percentage, visual loss continues for 6 weeks. Between 30% and 50% develop involvement of the fellow eye within months or years although this may be reduced with aspirin. When the second eye becomes involved, optic atrophy in one eye (Fig. 18.28a) and disc oedema in the other (Fig. 18.28b) gives rise to the 'pseudo-Foster Kennedy syndrome'.

> *NB:* AION never recurs in the same eye.

Arteritic anterior ischaemic optic neuropathy

Giant cell arteritis (GCA) (*see* Fig. 18.30b) is a medical emergency because prevention of blindness depends on prompt recognition and treatment. The disease typically affects patients older than 65 years and has a predilection for medium-sized and large arteries, particularly the superficial temporal, ophthalmic, posterior ciliary and the proximal part of the vertebral. The severity and extent of involvement are associated with the quantity of elastic tissue in the media and adventitia of the artery. For this reason, the intracranial arteries, which possess little elastic tissue, are usually spared. The four most important diagnostic criteria of GCA are: (a) jaw claudication, (b) neck pain, (c) C-reactive protein >2.45 mg/dl and ESR >47 mm/hour (*see* Chapter 20). Ocular complications of GCA include the following:

1. **Arteritic anterior ischaemic optic neuropathy** (AAION) is the most common (Fig. 18.29). In untreated patients the incidence is 30–50%, of which one-third develop bilateral involvement.
2. **Transient ischaemic attacks** (amaurosis fugax) may precede infarction of the optic nerve head.

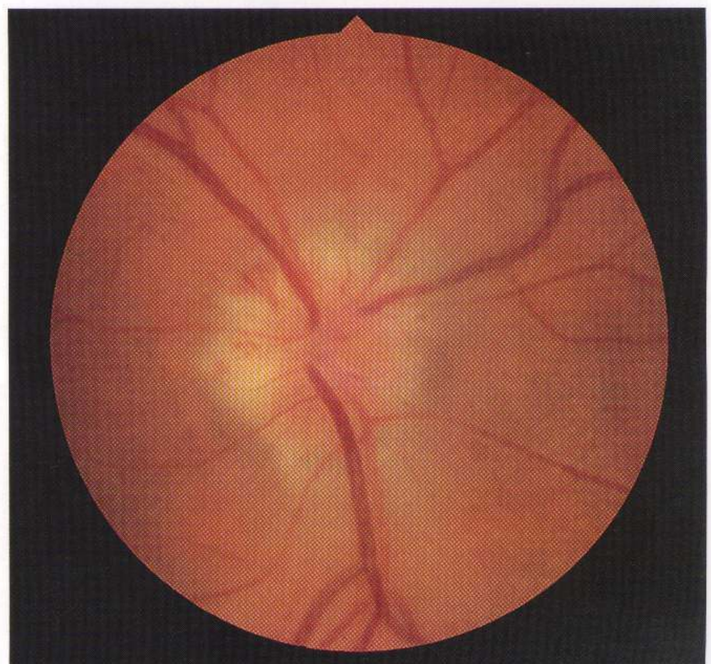


Fig. 18.29
Arteritic anterior ischaemic optic neuropathy

3. **Cotton wool spots** are uncommon. They are probably caused by platelet microembolization from the partially thrombosed ophthalmic or central retinal artery. Because GCA is a disease of medium-sized or large arteries, it does not involve terminal arterioles to produce cotton wool spots.
4. **Cilioretinal artery occlusion** may be combined with AAION (*see* Fig. 14.78).
5. **Central retinal artery occlusion** is usually combined with occlusion of a posterior ciliary artery. This is because the central retinal artery often arises from the ophthalmic artery by a common trunk with one or more of the posterior ciliary arteries. However, ophthalmoscopy shows occlusion of only the central retinal artery; the associated ciliary occlusion can be detected only on FA.
6. **Ocular ischaemic syndrome** due to involvement of the ophthalmic artery is rare (*see* Chapter 15).
7. **Diplopia**, transient or constant, may be caused by ischaemia of the ocular motor nerves or extraocular muscles.

Clinical features

1. **Presentation** is with sudden, profound unilateral visual loss which may be accompanied by periocular pain and preceded by transient visual obscurations and flashing lights. Bilateral simultaneous involvement is rare. Most cases occur within a few weeks of the onset of GCA although at presentation about 20% of patients do not have systemic symptoms (i.e. occult GCA).
2. **Signs** (in chronological order)
   - Pale and swollen optic disc with small splinter-shaped haemorrhages on its margin (Fig. 18.30a).
   - Over 1–2 months, the swelling gradually resolves (Fig. 18.30c) and severe optic atrophy ensues with profound impairment of visual function (Fig. 18.30d).
3. **FA** shows severe hypoperfusion of the choroid.
4. **Prognosis** is very poor because visual loss is usually permanent although, very rarely, prompt administration of systemic steroids may be associated with partial visual recovery.

Treatment

The aim of treatment is to prevent blindness of the fellow eye although, in a few unfortunate patients, the second eye also becomes blind despite prompt steroid administration.

1. **Regimen**
   - Intravenous methylprednisolone 1 g/day for 3 days together with oral prednisolone 80 mg daily.
   - After 3 days the oral dose is reduced to 60 mg and then 50 mg for 1 week each.
   - The daily dose is then reduced by 5 mg weekly; headache, ESR and C-reactive protein permitting, until 10 mg is reached.
   - Maintenance daily therapy is ideally 10 mg, although higher doses may be required to control headache.

> *NB:* Temporal artery biopsy should be performed, ideally within 3 days of starting treatment. Histological confirmation of GCA will justify long-term steroid administration.

2. **Duration** of treatment is governed by the patient's symptoms and the level of the ESR or C-reactive protein. Symptoms may, however, recur without a corresponding rise in ESR or C-reactive protein and vice versa. Most patients need treatment for 1–2 years, although some may require indefinite maintenance therapy.

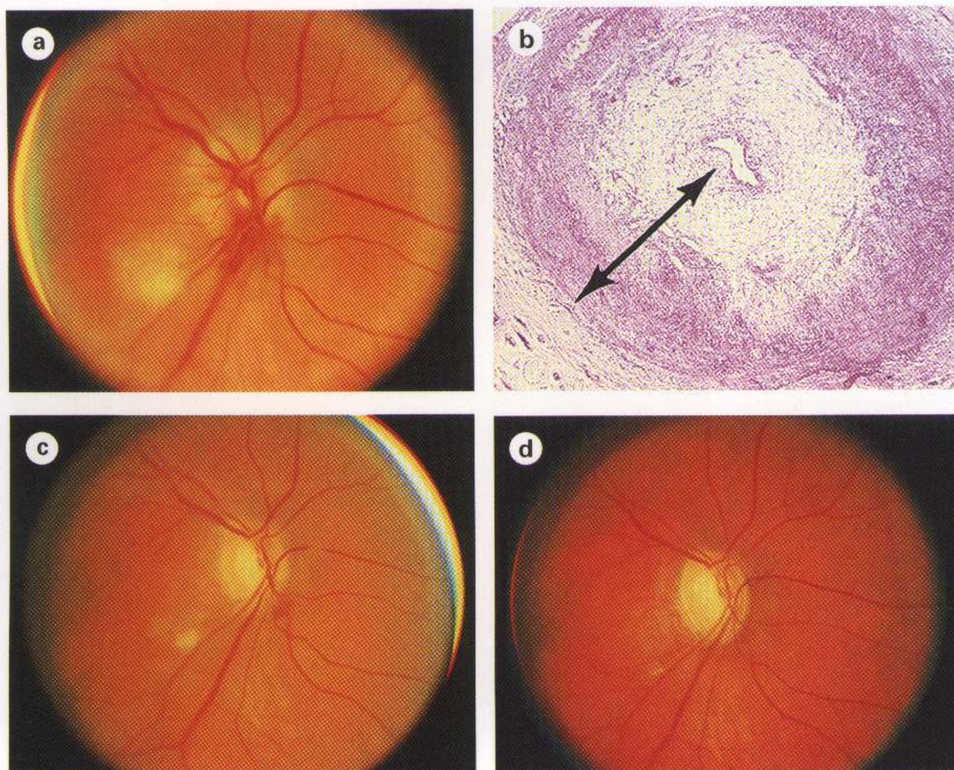


Fig. 18.30
Giant cell arteritis. (**a**, **c** and **d**) Progression of anterior ischaemic optic neuropathy (*see text*); (**b**) transverse section of an artery showing granulomatous inflammation involving all layers of the wall and constricting the lumen (arrows) (Courtesy of Wilmer Institute)

> *NB:* Injudicious use of steroids may cause greater harm than the disease itself. Steroid-induced complications may necessitate the use of steroid-sparing agents such as azathioprine.

Diabetic papillopathy

Diabetic papillopathy is an uncommon condition characterized by transient visual dysfunction associated with optic disc swelling which may occur in both type 1 and type 2 diabetics. The underlying pathogenesis is unclear but may be the result of small-vessel disease.

1. **Presentation** is usually with milder optic nerve dysfunction and slower progression than in NAION or optic neuritis.
2. **Signs**
   - Visual acuity is usually 6/12 or better.
   - Unilateral or bilateral, mild disc swelling and hyperaemia (Fig. 18.31).
   - Disc surface telangiectasia is common, and when severe may be mistaken for neovascularization on cursory examination.
   - Visual field defects in the form of generalized constriction or central scotomas.
   - Relative afferent pupillary defects may be seen in unilateral/asymmetric disease.
   - Dyschromatopsia may be present.
3. **Prognosis** is relatively good despite the lack of definitive treatment. Systemic steroids are of questionable benefit and tend to compromise diabetic control. In most cases spontaneous resolution occurs within several months, with stabilization or improvement of visual acuity, although mild optic atrophy may ensue.

Leber hereditary optic neuropathy

Leber hereditary optic neuropathy (LHON) is a rare disease which is the result of maternal mitochondrial DNA mutations (3460, 14484, 11778, and 15257). The majority of patients are males in their twenties with the 11778 mutation. In atypical cases the condition may affect females and present at any age between 10 and 60 years. The diagnosis of LHON should therefore be considered in any patient with bilateral optic neuritis, irrespective of age.

1. **Presentation** is typically with unilateral, acute, severe, painless visual loss. The fellow eye becomes similarly affected within days or weeks (but no longer than 2 months) after the first.
2. **Signs** during the acute stage are often subtle and easily overlooked; in some patients the disc may be entirely normal.
   - In typical cases there are dilated capillaries on the disc surface which may extend onto adjacent retina (telangiectatic microangiopathy), vascular tortuosity and swelling of the parapapillary nerve fibre layer (Fig. 18.32). Telangiectatic microangiopathy may be present in asymptomatic female relatives.
   - Subsequently, the telangiectatic vessels regress and severe optic atrophy ensues.

> *NB:* Surprisingly, the pupillary light reactions may remain fairly brisk.

3. **FA** shows absence of dye leakage.
4. **Visual field defects** usually consist of centrocaecal scotomas.
5. **Prognosis** is poor, although some visual recovery may occur in a minority of cases even years later. Most patients suffer severe, bilateral and permanent visual loss with a final visual acuity of 6/60 or less. The 11778 mutation carries the worst prognosis.

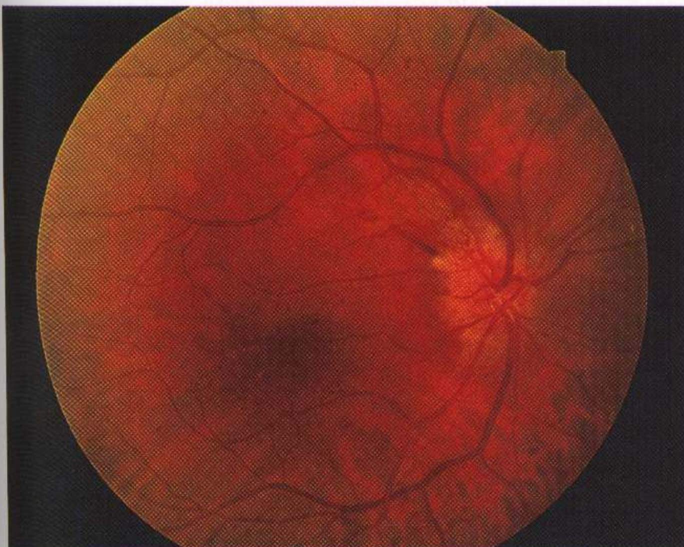


Fig. 18.31
Diabetic papillopathy

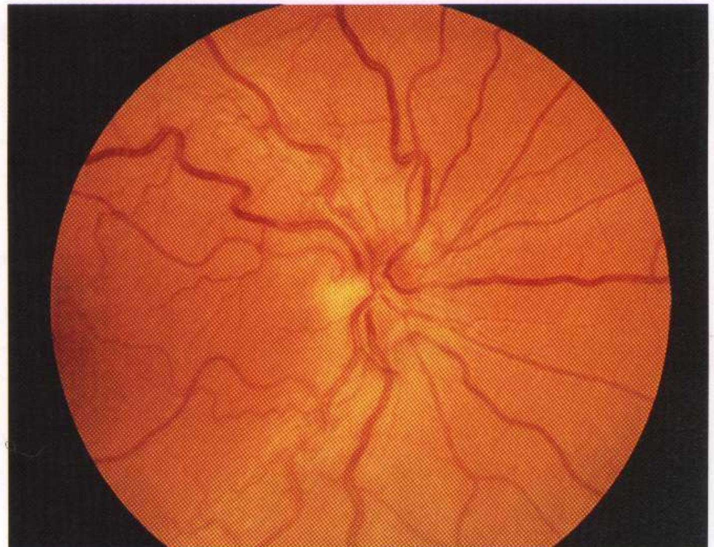


Fig. 18.32
Acute stage of Leber optic neuropathy

6. **Treatment** is generally ineffective although many modalities, including steroids, hydroxocobalamin and surgical intervention, have been tried. Smoking and excessive consumption of alcohol should be discouraged, to minimize potential stress on mitochondrial energy production.

Hereditary optic atrophies

The hereditary optic atrophies (neuropathies) are a very rare heterogeneous group of disorders that are primarily characterized by bilateral optic atrophy.

Kjer syndrome

1. **Inheritance** is AD.
2. **Presentation** is usually in the first decade with insidious visual loss.
3. **Signs**. Mild temporal or diffuse optic atrophy.
4. **Prognosis** is variable (final visual acuity 6/12–6/60) with considerable variation within and between families.
5. **Systemic abnormalities** are absent.

Behr syndrome

1. **Inheritance** is AR.
2. **Presentation** is in the first decade with visual loss which stabilizes after a variable period of progression.
3. **Signs**. Diffuse optic atrophy.
4. **Prognosis** is variable with moderate to severe visual loss and nystagmus.
5. **Systemic abnormalities** include spastic gait, ataxia and mental handicap.

Wolfram syndrome

This is also refered to as DIDMOAD = **D**iabetes **I**nsipidus, **D**iabetes **M**ellitus, **O**ptic **A**trophy and **D**eafness.

1. **Inheritance** is AR.
2. **Presentation** is between the ages of 5 and 21 years.
3. **Signs**. Diffuse optic atrophy.
4. **Prognosis** is very poor (final visual acuity is <6/60).

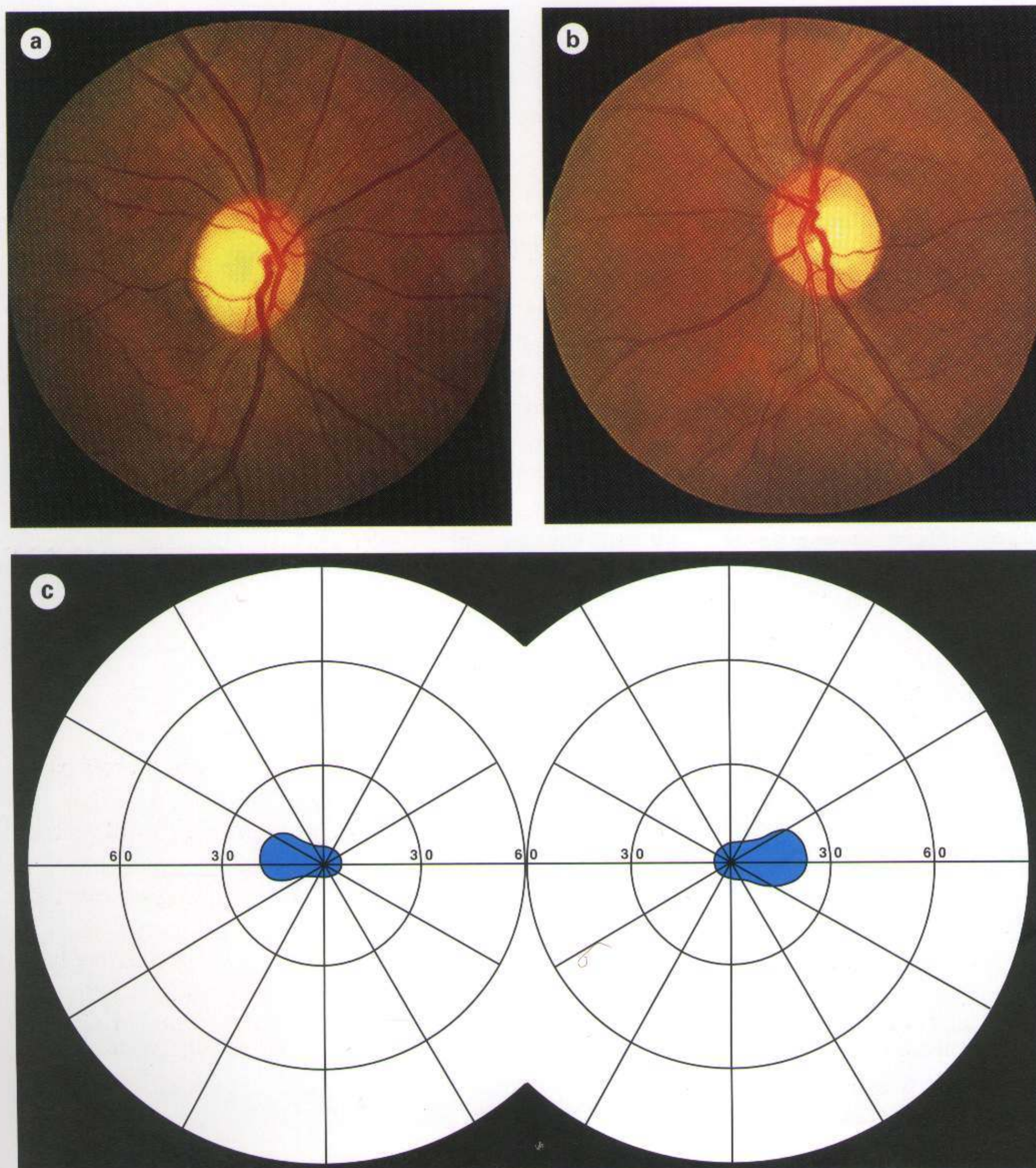


Fig. 18.33 Alcohol–tobacco amblyopia. (**a** and **b**) Temporal disc pallor; (**c**) bilateral centrocaecal scotomas (Courtesy of Wilmer Institute)

5. **Systemic abnormalities** (apart from DIDMOAD), include anosmia, ataxia, seizures, mental handicap, short stature, endocrine abnormalities and elevated CSF protein.

Alcohol–tobacco amblyopia

Alcohol–tobacco amblyopia typically affects heavy drinkers and cigar and pipe smokers who are deficient in protein and the B vitamins. Most patients have neglected their diet, obtaining their calories from alcohol instead.

1. **Presentation** is with insidious onset, progressive, bilateral, usually symmetrical visual impairment associated with dyschromatopsia.
2. **Signs**. The optic dics at presentation are normal in most cases. Some patients show subtle temporal pallor, splinter-shaped haemorrhages on or around the disc, or minimal disc oedema.
3. **Visual field defects** are bilateral, relatively symmetrical, centrocaecal scotomas (Fig. 18.33c). The margins of the defects are difficult to define with a white target but are easier to plot and larger when using a red target.
4. **Treatment** involves weekly injections of 1000 units of hydroxocobalamin for 10 weeks. Multivitamins are also administered and patients should be advised to eat a well-balanced diet and abstain from drinking and smoking.
5. **Prognosis** is good in early cases provided patients comply with treatment although visual recovery may be slow. In advanced and unresponsive cases there is permanent visual loss as a result of optic atrophy (Fig. 18.33a and b).

Drug-induced optic neuropathies

Ethambutol

Ethambutol (Myambutol, Mynah) is used in combination with isoniazid and rifampicin in the treatment of tuberculosis. Toxicity is dose- and duration-dependent, the incidence being 6% at a daily dose of 25 mg/kg; rarely 15 mg/kg may be toxic. Toxicity is unusual and may occur after 2 months of therapy (average is 7 months).

> *NB:* Isoniazid may also rarely cause toxic optic neuropathy, particularly in combination with ethambutol.

1. **Presentation** is with symmetrical insidious visual impairment associated with dyschromatopsia.
2. **Signs** include normal or slightly swollen optic discs with splinter-shaped haemorrhages.
3. **Visual field defects** usually consist of central or centrocaecal scotomas although bitemporal or peripheral constriction may occur.
4. **Prognosis** is good following cessation of treatment although recovery may take up to 12 months. A minority of patients develop permanent visual impairment as a result of optic atrophy.
5. **Screening** should be at about 3-monthly intervals if the daily dose exceeds 15 mg/kg. The drug should be stopped immediately if symptoms develop.

Amiodarone

Amiodarone is used to treat cardiac arrhythmias. Vortex keratopathy, which is innocuous, is virtually universal (*see* Chapter 5). Optic neuropathy, however, occurs in only 1–2% of patients and is not dose-related.

1. **Presentation** is with insidious unilateral or bilateral visual impairment.
2. **Signs** include bilateral optic disc swelling that stabilizes within several months of discontinuing medication.
3. **Visual field defects** may be mild and reversible or severe and permanent.
4. **Prognosis** is variable because cessation of the drug may not bring about improvement.
5. **Screening** is not appropriate because there is no way to identify those at risk. Patients should, however, be warned of the small risk of toxicity and advised to report any suggestive symptoms.

Vigabatrin

Vigabatrin is an antiepileptic drug, used mainly as second-line therapy, except in infantile spasms (West syndrome). A significant percentage of patients develop dyschromatopsia and constricted visual fields when the total dose is 1500 g or more. The defects develop within 1 month and several years of starting therapy and are often permanent despite discontinuation of the drug. Product literature advises visual field testing at six monthly intervals.

Raised intracranial pressure

Introduction

Cerebrospinal fluid

1. **Circulation** (Fig. 18.34a)
   - Cerebrospinal fluid (CSF) is formed by the choroid plexus in the ventricles of the brain.
   - It leaves the lateral ventricles to enter the third ventricle through the foramina of Munro.
   - From the third ventricle, it flows through the sylvian aqueduct to the fourth ventricle.
   - From the fourth ventricle, the CSF passes through the foramina of Luschka and Magendie to enter the subarachnoid space, some flowing around the spinal cord and the rest bathing the cerebral hemispheres.
   - Absorption is into the cerebral venous drainage system through the arachnoid villi.

2. **Normal opening pressure** of CSF on lumbar puncture is <80 mm H_2O in infants, <90 mm in children and <210 mm in adults.

Causes of raised intracranial pressure (Fig. 18.34b)

1. **Obstruction** of the ventricular system by congenital or acquired lesions.
2. **Space-occupying** intracranial lesions, including haemorrhage.
3. **Impairment** of CSF absorption via arachnoid villi, which may be damaged by meningitis, subarachnoid haemorrhage or cerebral trauma.
4. **Idiopathic intracranial hypertension** (pseudo-tumour cerebri).
5. **Diffuse cerebral oedema** from blunt head trauma.
6. **Severe systemic hypertension.**
7. **Hypersecretion of CSF** by choroid plexus tumour, which is very rare.

Hydrocephalus

Hydrocephalus is dilatation of the ventricles (Fig. 18.35). Raised intracranial pressure may be associated with two types of hydrocephalus.

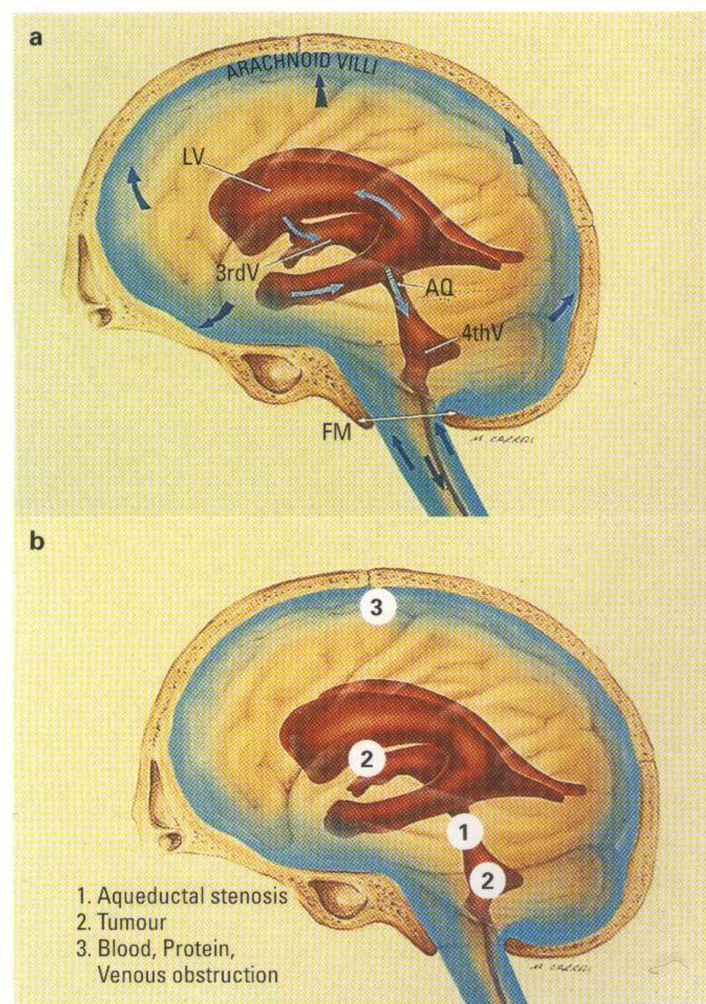


Fig. 18.34
(a) Circulation of cerebrospinal fluid (*see text*); **(b)** causes of elevation of intracranial pressure (*see text*) (Courtesy of Wilmer Institute)



Fig. 18.35
Axial CT scan showing severe hydrocephalus (Courtesy of K. Nischal)

1. **Communicating hydrocephalus**, in which the CSF flows from the ventricular system to the subarachnoid space without impediment. The obstruction to flow lies in the basilar cisterns or in the subarachnoid space, where there is failure of absorption by the arachnoid villi.
2. **Non-communicating hydrocephalus** is caused by obstruction to CSF flow in the ventricular system or at the exit foramina of the fourth ventricle. The CSF therefore does not have access to the subarachnoid space.

Clinical features

Systemic

1. **Headaches** may come on at any time of day but characteristically occur early in the morning and may wake the patient from sleep. They tend to get progressively worse and patients usually present to hospital within 6 weeks. The headaches may be generalized or localized, and may intensify with head movement, bending or coughing. Patients with lifelong headaches often report a change in character of the headache. Very rarely, headache may be absent.
2. **Sudden nausea and vomiting**, often projectile, may partially relieve the headache. Vomiting may occur as an isolated feature or may precede the onset of headaches by months, particularly in patients with fourth ventricular tumours.
3. **Deterioration of consciousness** may be slight, with drowsiness and somnolence. Dramatic deterioration of consciousness is indicative of brain stem distortion and tentorial or tonsillar herniation and requires prompt attention.

Visual

1. **Transient visual obscurations** lasting a few seconds are frequent in patients with papilloedema.

2. **Horizontal diplopia** is caused by stretching of the sixth nerve over the petrous tip. It is therefore a false localizing sign.
3. **Visual failure** occurs late in patients with secondary optic atrophy due to long-standing papilloedema (*see* below).

Papilloedema

Introduction

By definition, papilloedema is swelling of the optic nerve head, secondary to raised intracranial pressure. It is nearly always bilateral, although it may be asymmetrical. All other causes of disc oedema in the absence of raised intracranial pressure are referred to as 'disc swelling' and usually produce visual impairment. All patients with papilloedema should be suspected of having an intracranial mass unless proved otherwise (Fig. 18.36). However, not all patients with raised intracranial pressure will necessarily develop papilloedema. Tumours of the cerebral hemispheres tend to produce papilloedema later than those in the posterior fossa. Patients with a history of previous papilloedema may develop a substantial increase in intracranial pressure but fail to redevelop papilloedema because of glial scarring of the optic nerve head.

Clinical features

1. **Early papilloedema** (Fig. 18.37) may be difficult to diagnose with certainty. The following are its main features:

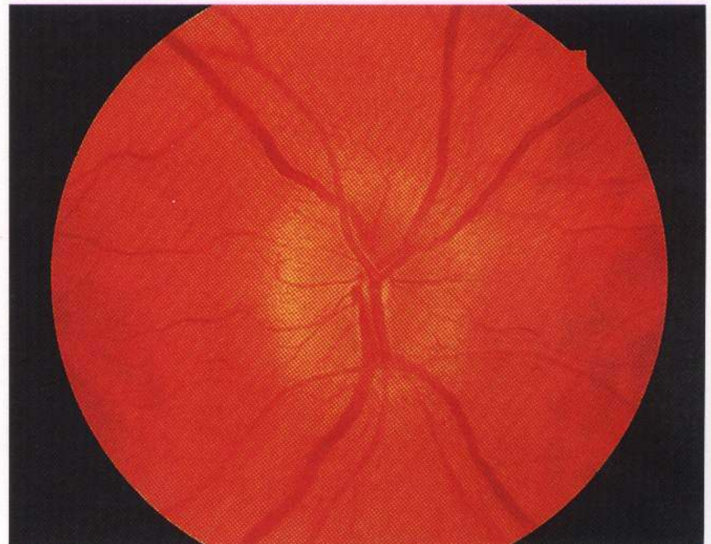


Fig. 18.37
Early papilloedema

- Visual symptoms are absent and visual acuity is normal.
- Optic discs show hyperaemia and mild elevation.
- The disc margins (initially nasal, later superior, inferior and temporal) appear indistinct, and swelling of the parapapillary retinal nerve fibre layer develops.
- There is loss of previous spontaneous venous pulsation. However, as about 20% of normal individuals do not manifest spontaneous venous pulsation, its absence does not necessarily imply raised intracranial pressure.

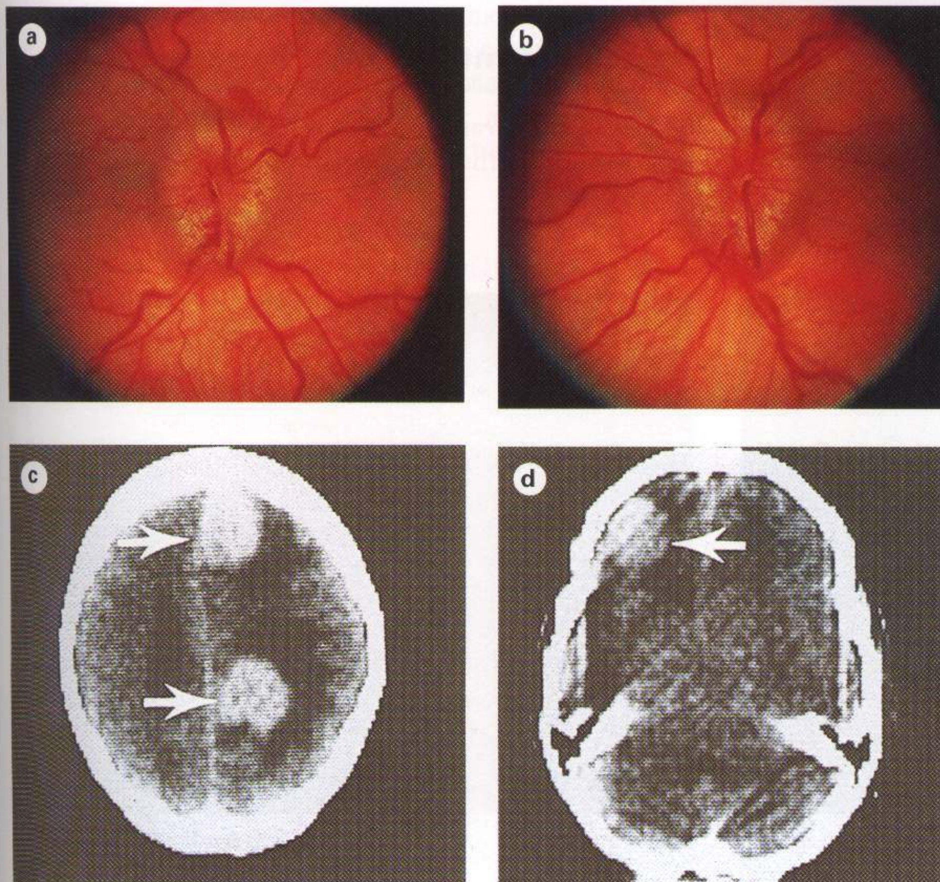
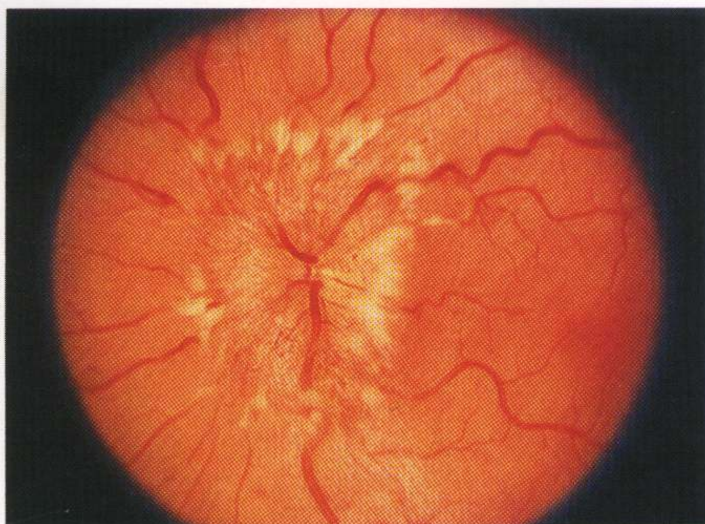


Fig. 18.36
(**a** and **b**) Papilloedema; (**c**) CT scan showing two metastases; (**d**) CT scan at a different level showing a third metastasis
(Courtesy of Wilmer Institute)


Fig. 18.38
Established papilloedema

Preserved venous pulsation renders the diagnosis of papilloedema unlikely.

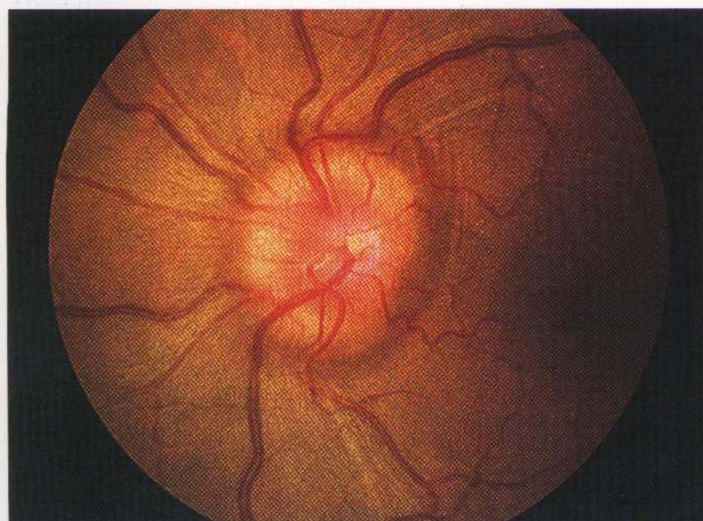
2. **Established papilloedema** (Fig. 18.38)
   - Transient visual obscurations may occur in one or both eyes, lasting a few seconds, often on standing.
   - Visual acuity is normal or reduced.
   - Optic discs show severe hyperaemia, and moderate elevation with indistinct margins, which may initially be asymmetrical.
   - The optic cup and the small vessels on the disc are obscured.
   - Venous engorgement, parapapillary flame-shaped haemorrhages and frequently also cotton wool spots may be seen.
   - As the swelling increases, the optic nerve head appears enlarged; circumferential retinal folds may develop on its temporal side.
   - Hard exudates may radiate from the centre of the fovea in the form of a 'macular fan': an incomplete star with the temporal part missing.
   - The blind spot is enlarged.
3. **Long-standing (vintage) papilloedema** (Fig. 18.39)
   - Visual acuity is variable and the visual fields begin to constrict.
   - Optic discs are markedly elevated with a 'champagne cork' appearance.
   - Cotton wool spots and haemorrhages are absent.
   - Opticociliary shunts and drusen-like crystalline deposits (corpora amylacea) may be present on the disc surface.
4. **Atrophic papilloedema (secondary optic atrophy)** (Fig. 18.40)
   - Visual acuity is severely impaired.
   - The optic discs are a dirty grey colour, slightly elevated, with few crossing blood vessels and indistinct margins.

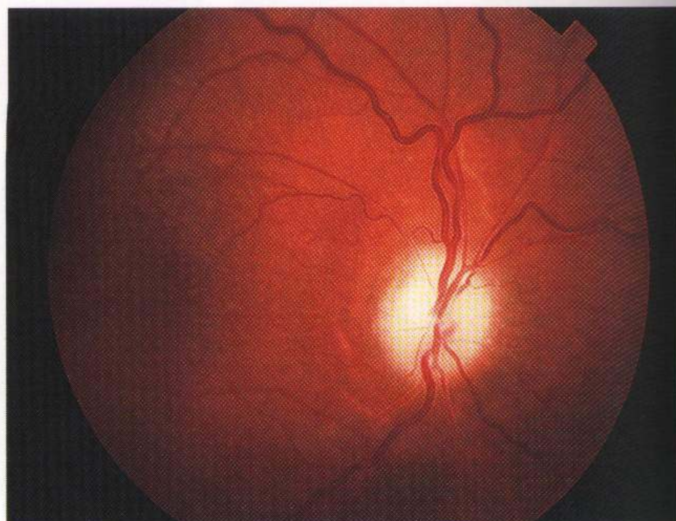
Differential diagnosis

1. **Buried drusen** may be mistaken for early papilloedema (*see* later).
2. **Bilateral disc swelling** may be caused by:
   - Malignant hypertension.
   - Bilateral papillitis.
   - Bilateral compressive thyroid ophthalmopathy.
   - Bilateral simultaneous anterior ischaemic optic neuropathy.
   - Bilaterally compromised venous drainage in central retinal vein occlusion or carotid–cavernous fistula.

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (IIH) deserves special mention, since the ophthalmologist may be involved in


Fig. 18.39
Long-standing papilloedema


Fig. 18.40
Atrophic papilloedema

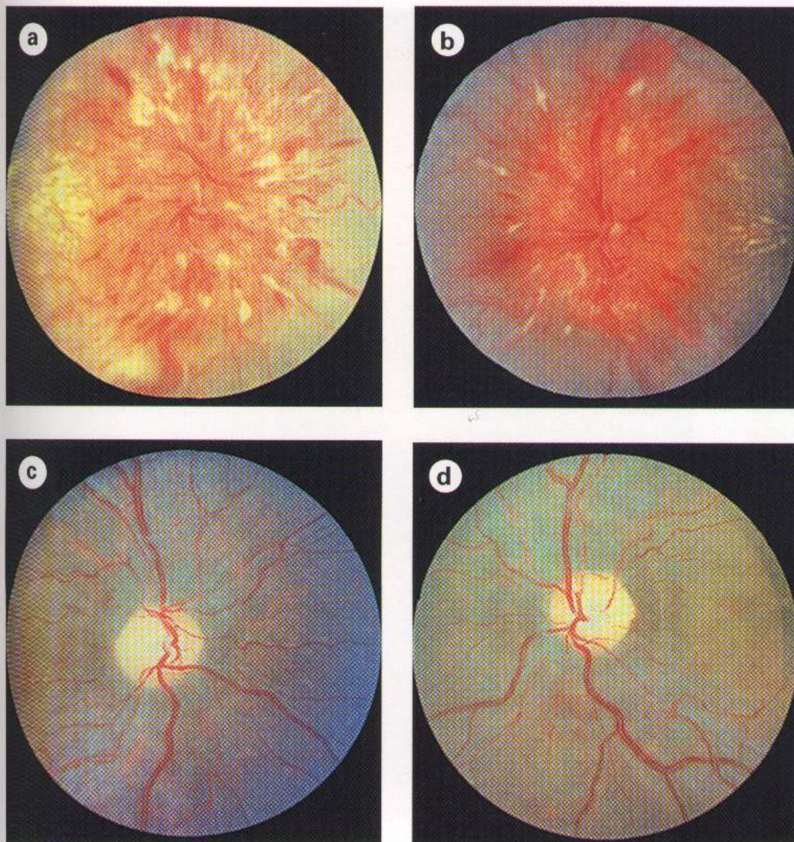


Fig. 18.41
(**a** and **b**) Severe papilloedema in idiopathic intracranial hypertension; (**c** and **d**) mild optic atrophy following resolution (Courtesy of Wilmer Institute)

management. It is defined as the presence of raised intracranial pressure in the absence of an intracranial mass lesion or enlargement of the ventricles due to hydrocephalus. Although not life-threatening IIH may result in permanent visual damage due to papilloedema. Ninety per cent of patients are obese women of child-bearing age, who are often amenorrhoeic. Intracranial hypertension may also be caused by drugs including tetracyclines, nalidixic acid and iron therapy.

Clinical features

1. **Signs and symptoms** of raised intracranial pressure as described above.
2. **Lumbar puncture** shows an opening pressure of >210 mm H_2O. However, it may be artefactually raised in obese patients with normal intracranial pressure.
3. **Neuroimaging** shows normal or small and slit-like ventricles.
4. **Course**. Most patients have a prolonged course with spontaneous relapses and remissions, although a few may have a short course lasting only a few months. Although mortality is low, visual loss, sometimes severe, is common (Fig. 18.41).

Management

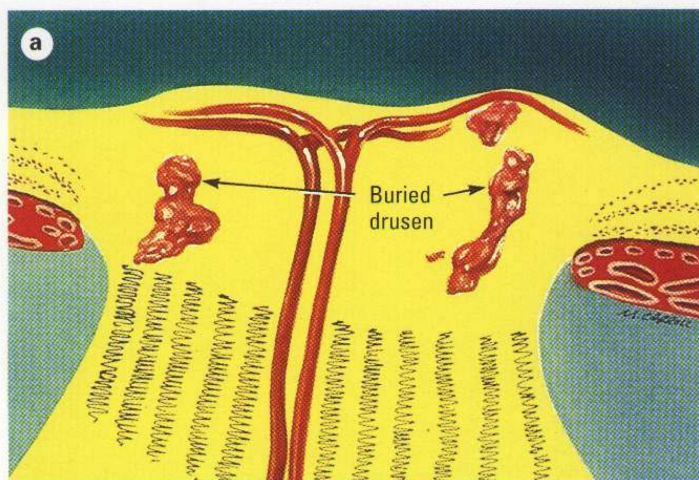
The two main aims are to relieve headaches and to prevent visual loss.

1. **Regular perimetry** is essential to detect early or progressive visual field loss.
2. **Diuretics** such as acetazolamide or thiazides usually relieve headache but their effects on preservation of visual function are unclear.
3. **Systemic steroids** are often used short term but are unsatisfactory for chronic administration because of their potential complications, particularly in obese patients.
4. **Optic nerve fenestration**, which involves incision of the meningeal sheath around the optic nerve, is safe and effective in preserving vision provided it is performed early. However, headache is relieved only in a minority of cases.
5. **Lumboperitoneal shunts** may be performed but the failure rate is high and surgical revision is frequently required.

Congenital optic nerve anomalies with neurological associations

Optic disc drusen

Optic disc drusen (hyaline bodies) are composed of hyaline-like calcific material within the substance of the optic nerve head (Fig. 18.42). Clinically, they are present in about 0.3% of the population and are often bilateral. Although only a minority of family members have disc drusen nearly half



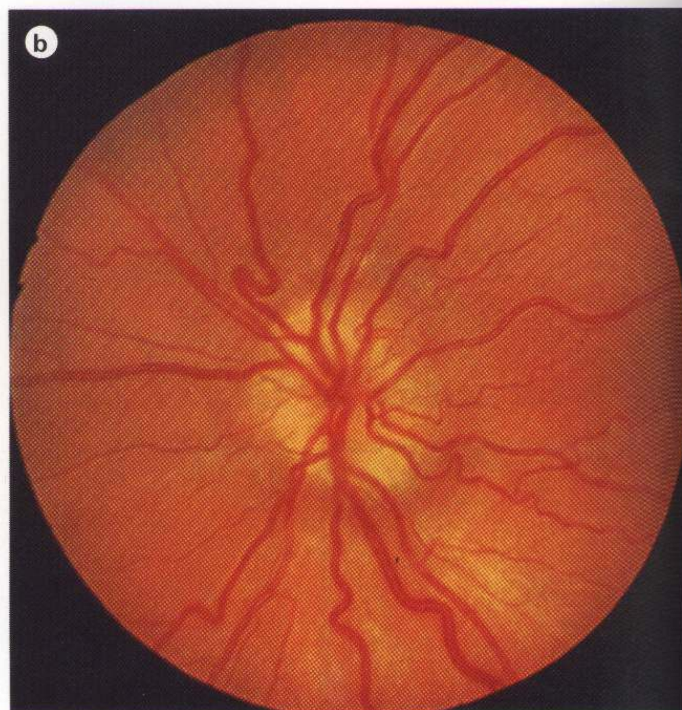
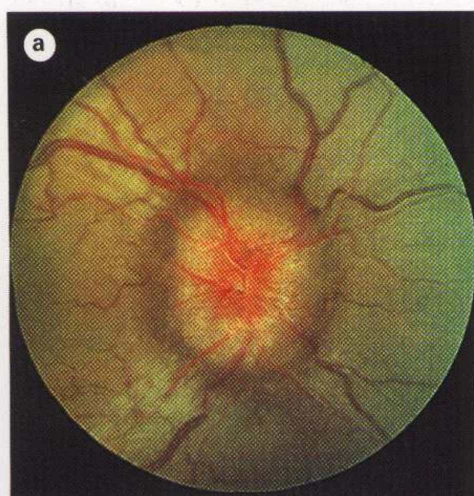
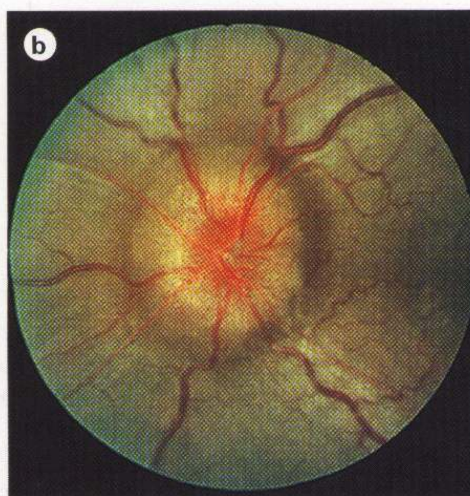
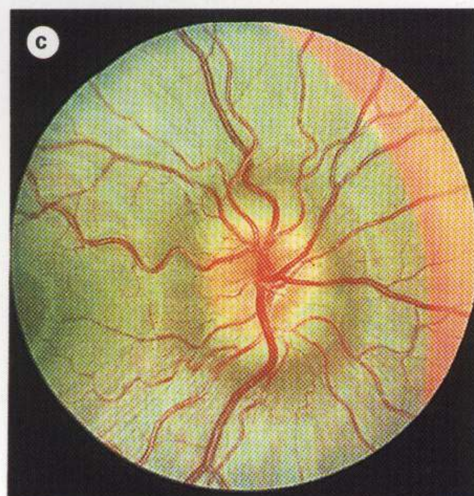


Fig. 18.42
Buried optic disc drusen (*see text*) (Courtesy of Wilmer Institute)







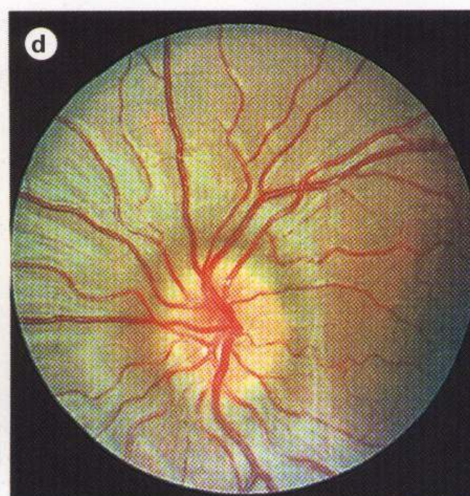


Fig. 18.43
(**a** and **b**) Long-standing papilloedema; (**c** and **d**) buried optic disc drusen (*see text*) (Courtesy of Wilmer Institute)

manifest anomalous disc vessels and absence of the physiological optic cup.

Clinical features

1. **Buried drusen**. In early childhood drusen may be difficult to detect because they lie deep beneath the surface of the disc (Fig. 18.43c and d). In this setting the appearance may mimic papilloedema (Fig. 18.43a and b). Signs suggestive of disc drusen are:
   - Elevated disc with a scalloped margin without a physiological cup.
   - Absence of hyperaemia of the disc surface.
   - The surface vessels are not obscured, despite the disc elevation.
   - Anomalous vascular patterns including early branching, increased number of major retinal vessels and vascular tortuosity.
   - Spontaneous venous pulsation may be present in 80% of cases.
2. **Exposed drusen**. During the early teens drusen usually emerge at the surface of the disc as waxy pearl-like irregularities (Fig. 18.44).
3. **Complications** are uncommon.
   - A small minority of patients develop visual impairment as a result of juxtapapillary choroidal neovascularization (Fig. 18.45).
   - Occasionally a progressive but limited loss of visual field with a nerve fibre bundle pattern may occur.
4. **Associations** include retinitis pigmentosa, angioid streaks and Allagille syndrome.

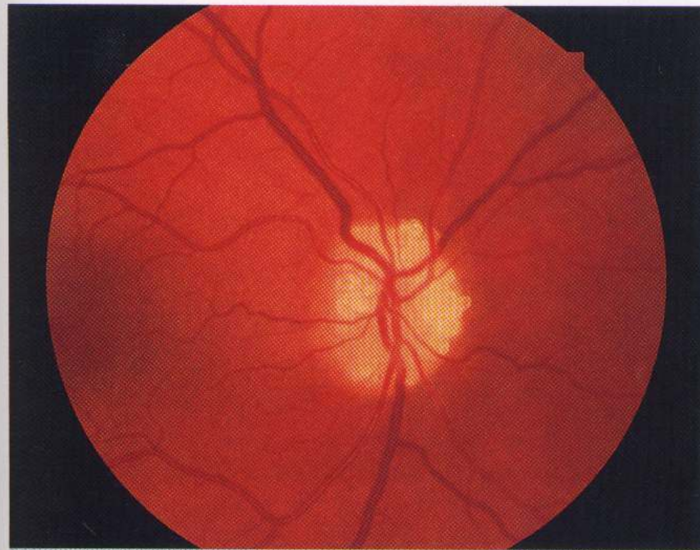
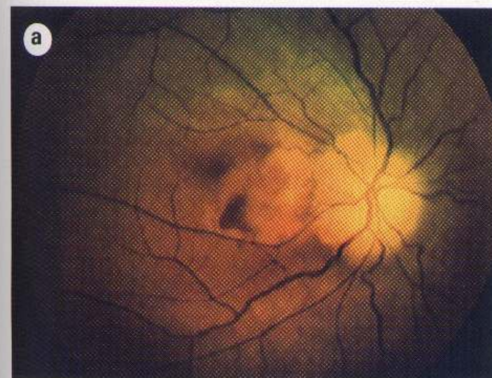


Fig. 18.44
Exposed optic disc drusen

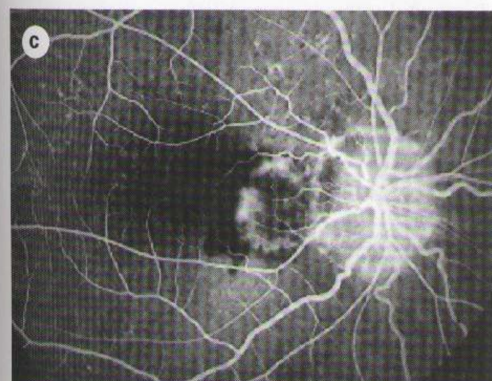
Special investigations

The following may be necessary for the definitive diagnosis of disc drusen, particularly when buried:

1. **Ultrasonography** (Fig. 18.46) is the most readily available and reliable method because of its ability to detect calcific deposits. With the gain turned down, drusen can still be recognized by their high acoustic reflectivity.
2. **CT** (Fig. 18.47) is less sensitive than ultrasonography and may miss small drusen. Drusen may, however, be detected incidentally on CT, when performed in the course of investigation of other pathology.







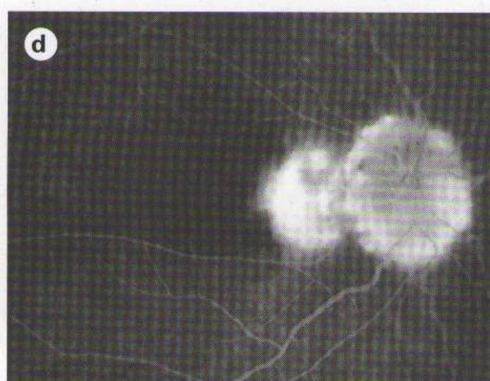


Fig. 18.45
(a) Optic disc drusen associated with macular oedema and haemorrhage; **(b)** autofluorescence of drusen; **(c)** early venous phase FA showing parapapillary choroidal neovascularization; **(d)** late phase showing hyperfluorescence due to leakage (Courtesy of S. Milewski)

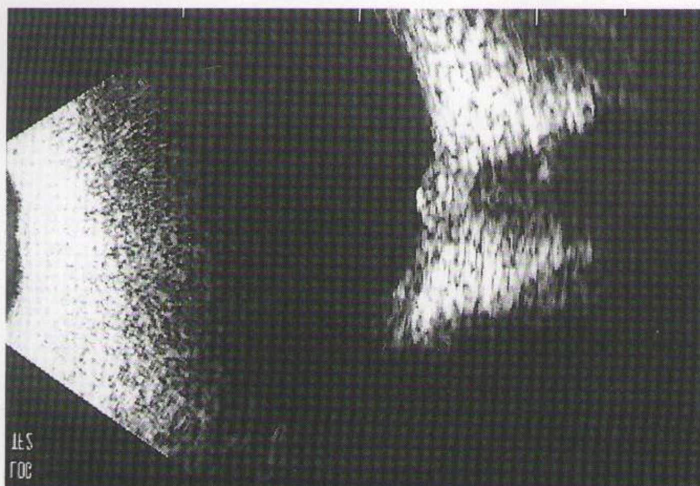


Fig. 18.46
B scan ultrasonogram of optic disc drusen



Fig. 18.47
Axial CT scan of optic disc drusen

3. **FA** may occasionally be helpful and shows the following:
   - Exposed drusen (Fig. 18.48a and b) show the phenomenon of autofluorescence prior to dye injection (Fig. 18.48c) and late localized hyperfluorescence due to staining (Fig. 18.48d). However, these phenomena may not be prominent with buried drusen because of attenuation from the overlying tissue (Fig. 18.49).

> *NB:* FA in papilloedema shows increasing hyperfluorescence and late leakage (Fig. 18.50).

Optic disc coloboma

An optic disc coloboma results from incomplete closure of the choroidal fissure. It is a rare condition, mostly sporadic, although AD inheritance may occur. Optic disc colobomas occur unilaterally or bilaterally with equal frequency and may have profound systemic implications.

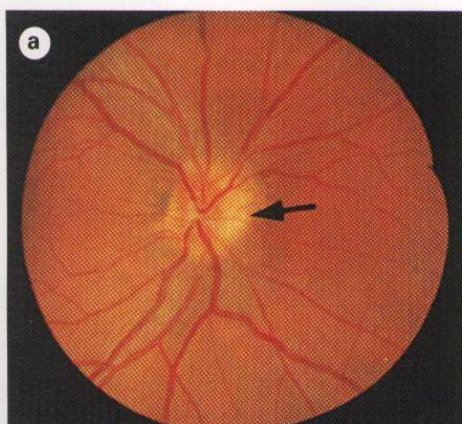
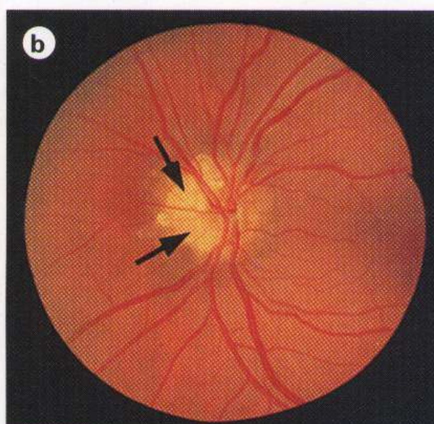
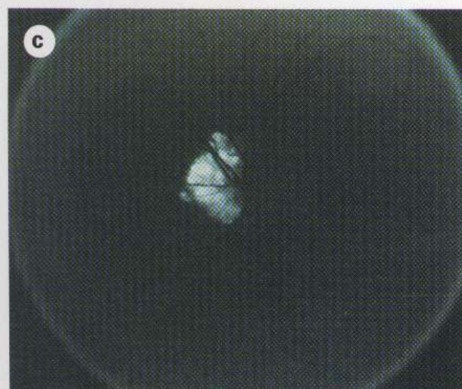
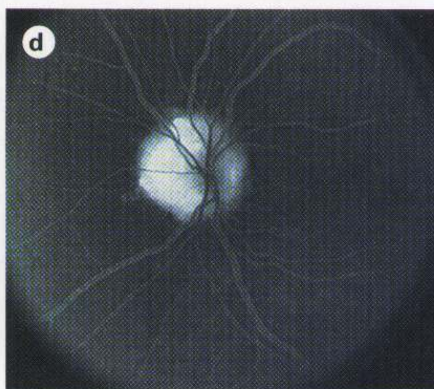
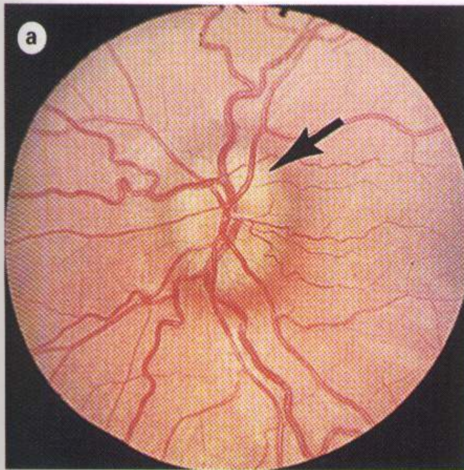
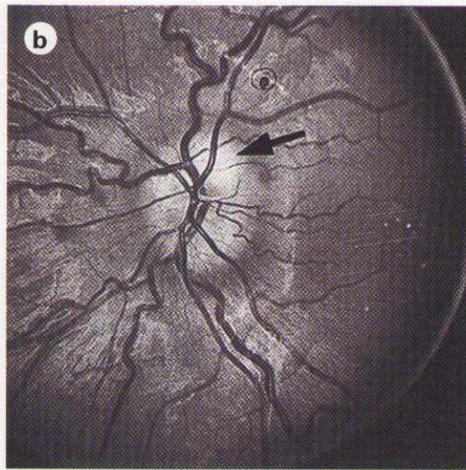
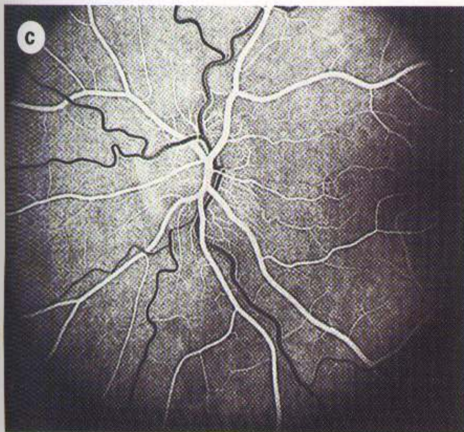





Fig. 18.48
(**a** and **b**) Exposed optic disc drusen; (**c**) autofluorescence; (**d**) late phase FA showing marked hyperfluorescence confined to the disc due to staining without leakage
(Courtesy of Wilmer Eye Institute)







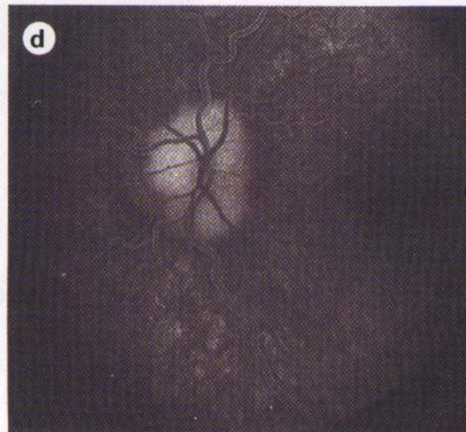
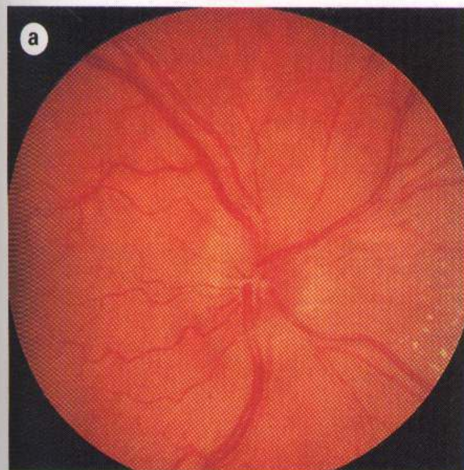
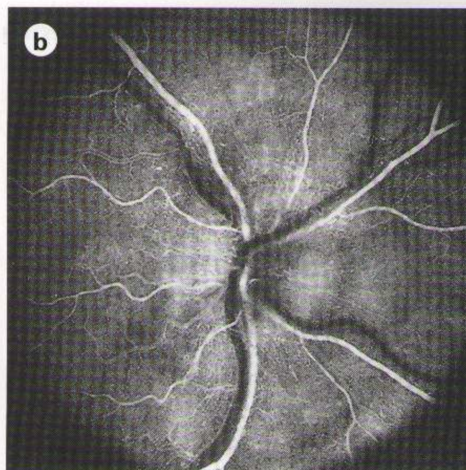
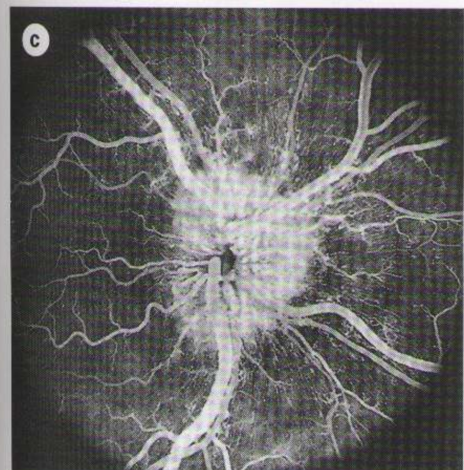


Fig. 18.49
(**a**) Buried optic disc drusen (arrow); (**b**) red-free photograph; (**c**) arterial phase FA is normal; (**d**) late phase showing mild hyperfluorescence confined to the disc (Courtesy of Wilmer Institute)







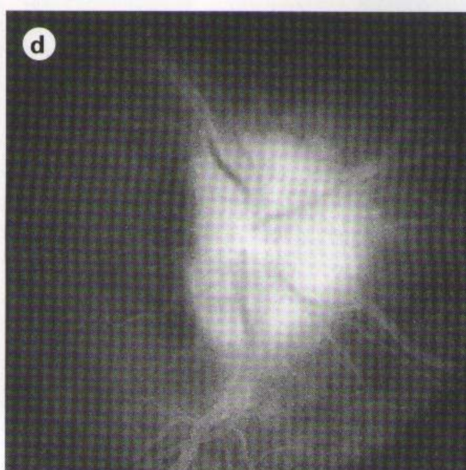


Fig. 18.50
(**a**) Papilloedema; (**b**) arterial phase FA showing congested parapapillary capillaries along the retinal nerve fibre layer; (**c**) arteriovenous phase showing increased hyperfluorescence of dilated capillaries extending to adjacent retina; (**d**) late phase showing marked hyperfluorescence due to leakage (Courtesy of A. Chopdar)

Clinical features

1. Signs
- Visual acuity is often decreased.
- The disc shows a discrete, focal, glistening, white, bowl-shaped excavation, decentred inferiorly so that the inferior neuroretinal rim is thin or absent and normal disc tissue is confined to a small superior wedge (Fig. 18.51a).
- The optic disc itself may be enlarged.
- Retinal vasculature is normal.

2. Visual fields show a superior defect (Fig. 18.51b) which, in conjunction with the disc appearance, may be mistaken for normal-tension glaucoma.

3. Ocular associations include microphthalmos and colobomas of iris (*see* Fig. 18.54), ciliary body and fundus (Fig. 18.52).

4. Complications
- Serous retinal detachment at the macula may occur (*see* Fig. 18.51a).
- Progressive enlargement of the excavation and neural rim thinning despite normal intraocular pressure has been described.
- Rhegmatogenous retinal detachment may occur in eyes with associated chorioretinal colobomas.

Systemic associations

These are numerous. Only the most important will be mentioned.

1. **Chromosomal anomalies** include Patau syndrome (trisomy 13), Edward syndrome (trisomy 18) and Cat-eye syndrome (trisomy 22).
2. **'CHARGE'** association comprises **C**oloboma, **H**eart defects, choanal **A**tresia, **R**etarded growth and development, **G**enital and **E**ar anomalies.

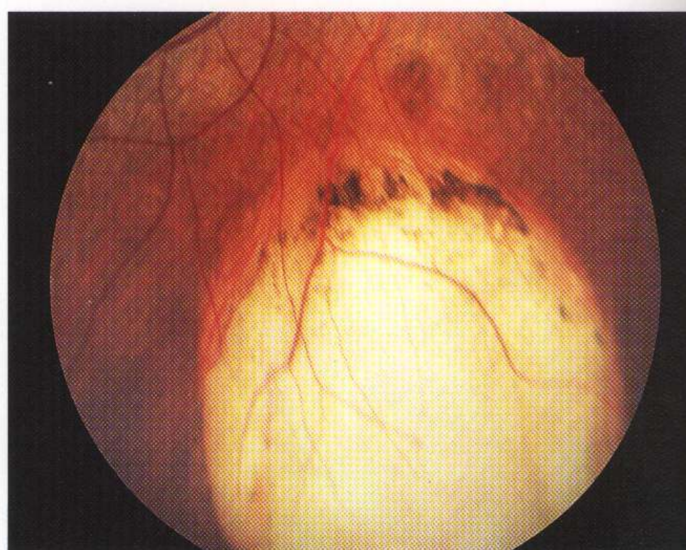


Fig. 18.52
Chorioretinal coloboma

3. **Other syndromes** include Meckel–Gruber, Goltz, Lenz microphthalmos, Walker–Warburg, Goldenhar, Dandy–Walker cyst and Rubinstein–Taybi.

Morning glory anomaly

Morning glory anomaly is a very rare, usually unilateral sporadic condition. Bilateral cases, which are rarer still, may be hereditary.

Clinical features

1. Signs
- Visual acuity is usually very poor.
- The disc is enlarged and manifests a funnel-shaped excavation (Fig. 18.53).

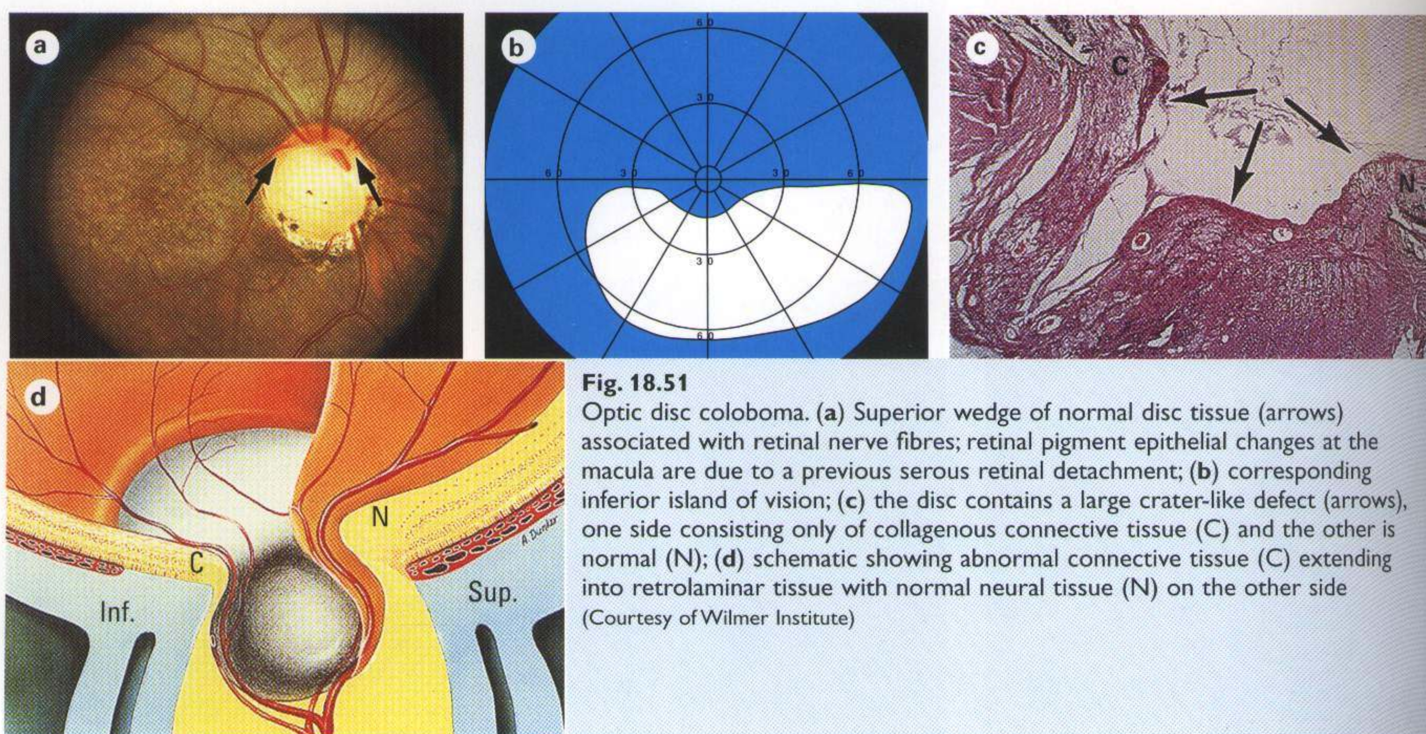


Fig. 18.51
Optic disc coloboma. (**a**) Superior wedge of normal disc tissue (arrows) associated with retinal nerve fibres; retinal pigment epithelial changes at the macula are due to a previous serous retinal detachment; (**b**) corresponding inferior island of vision; (**c**) the disc contains a large crater-like defect (arrows), one side consisting only of collagenous connective tissue (C) and the other is normal (N); (**d**) schematic showing abnormal connective tissue (C) extending into retrolaminar tissue with normal neural tissue (N) on the other side
(Courtesy of Wilmer Institute)

- A central core of whitish glial tissue, representing persistent hyaloid remnants lies at the base of the excavation.
- The disc is surrounded by an elevated annulus of chorioretinal pigmentary disturbance.
- The blood vessels emerge from the rim of the excavation in a radial pattern like the spokes of a wheel. They are increased in number and it is difficult to distinguish arteries from veins.

2. **Complication**. Serous retinal detachment develops in about 30% of cases.

Systemic associations

Uncommon systemic associations include the following:

1. **Frontonasal dysplasia**, the most important, is characterized by a malformation complex consisting of:
   - Mid-facial anomalies including hypertelorism, depressed nasal bridge (Fig. 18.54) hare lip and cleft palate.
   - Basal encephalocele (Figs 18.55 and 18.56), absent corpus callosum and pituitary deficiency.
2. **Neurofibromatosis type 2** is a rare association.

Optic nerve hypoplasia

The hypoplastic optic nerve, unilateral or bilateral, is characterized by a diminished number of nerve fibres. It may occur as an isolated anomaly in an otherwise normal eye, in a grossly malformed eye or in association with a heterogeneous group of disorders most commonly involving the midline structures of the brain. Specific agents used by the mother during gestation which may be associated with optic nerve hypoplasia include alcohol, LSD, quinine, protamine zinc insulin, steroids, diuretics, cold remedies and anticonvulsants. Superior segmental hypoplasia may be associated with maternal diabetes.

Clinical features

1. **Signs**
   - Visual acuity can vary from normal to no light perception.

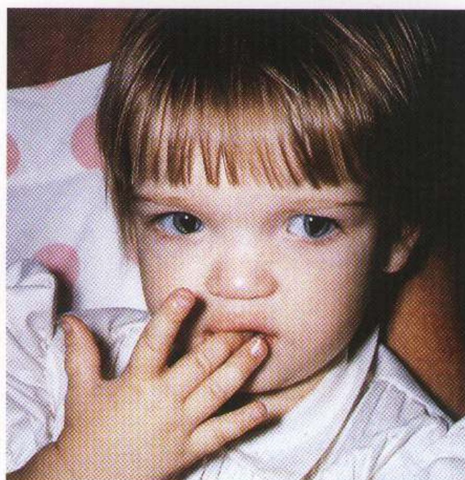


Fig. 18.54
A patient with iris colobomas, hypertelorism and a depressed nasal bridge

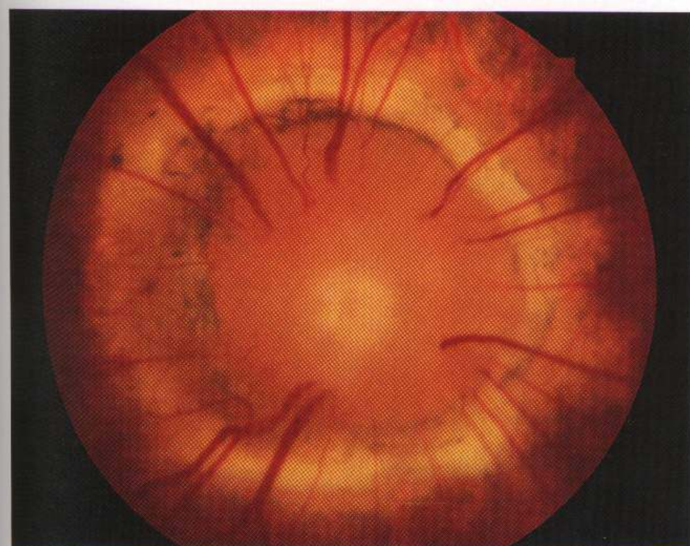


Fig. 18.53
Morning glory anomaly

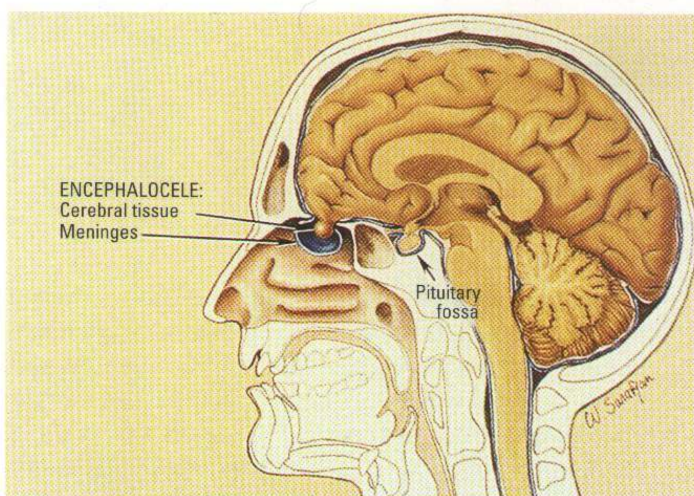
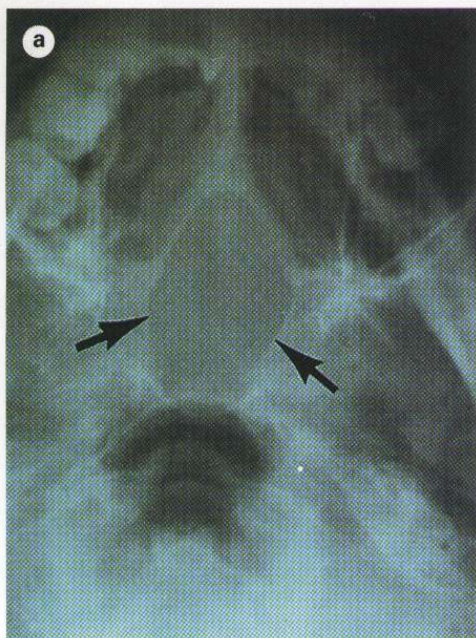


Fig. 18.55
Basal encephalocele (Courtesy of Wilmer Institute)



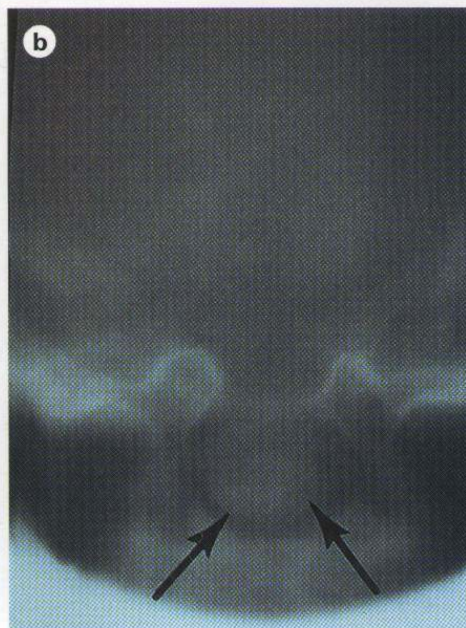
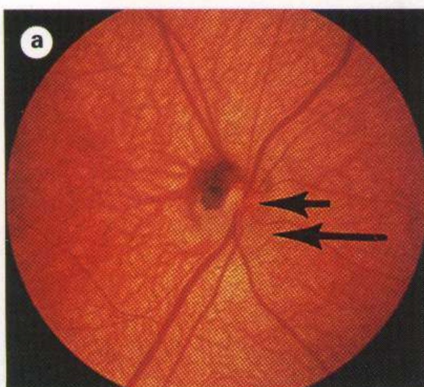
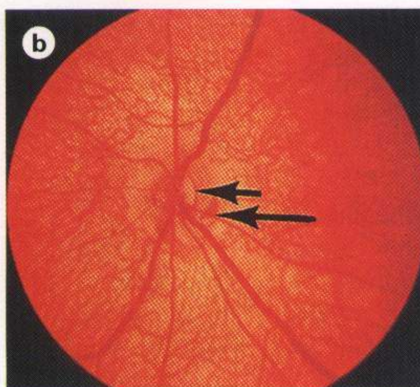
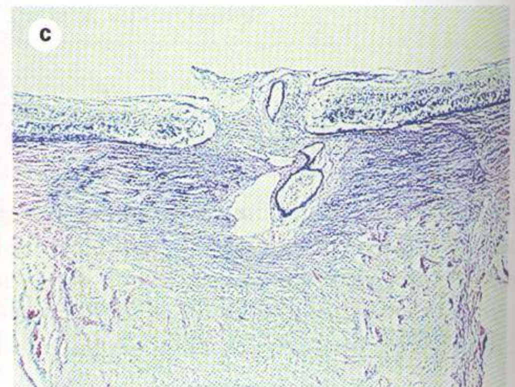


Fig. 18.56
Basal encephalocele. (**a**) Defect on the bony floor of the skull (arrows); (**b**) soft tissue protruding through the defect (arrows) (Courtesy of Wilmer Institute)







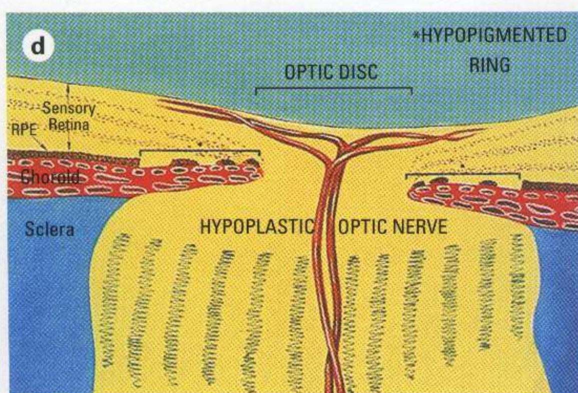
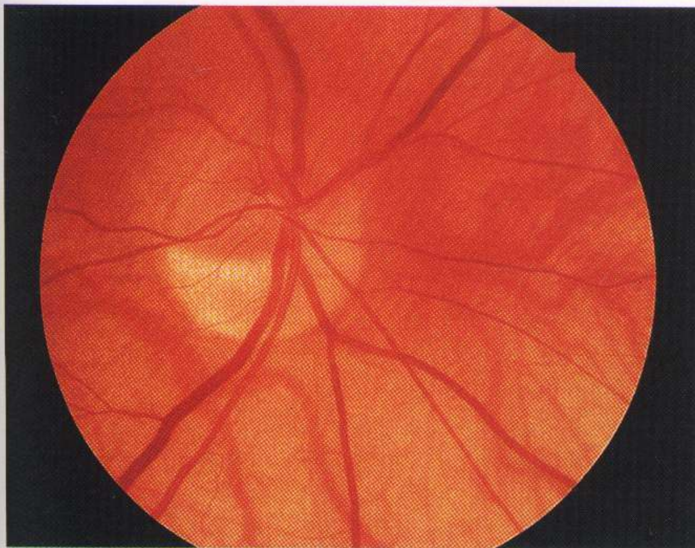


Fig. 18.57
Optic nerve hypoplasia. (**a** and **b**) Disc outline (short arrow), hypopigmented ring (long arrow); (**c**) longitudinal section showing hypoplasia of the disc and retrolaminar optic nerve; (**d**) hypopigmented ring due to absence of the retinal pigment epithelium (Courtesy of Wilmer Institute)

- The disc is small and grey and is surrounded by a yellow halo of hypopigmentation caused by concentric chorioretinal atrophy (double-ring sign) (Fig. 18.57). The outer ring represents what would have been the normal disc margin.
- The distance from the fovea to the temporal border of the optic disc often equals or exceeds three times the disc diameter. This strongly suggests disc hypoplasia.
- Despite the small size of the disc, the retinal blood vessels are of normal calibre, although they may be tortuous.
- In some cases only a part of the disc is hypoplastic (Fig. 18.58).

2. Other features vary considerably, depending on the severity. They include field defects, dyschromatopsia, afferent pupillary defect, foveal hypoplasia, aniridia, microphthalmos, strabismus and nystagmus in severe bilateral cases. Mild cases can be easily overlooked; the slight reduction of visual acuity may be mistaken for amblyopia and treated by occlusion.


Fig. 18.58
Sectoral optic disc hypoplasia

Systemic associations

1. **de Morsier syndrome** (septo-optic dysplasia) is present in about 10% of cases. In addition to bilateral optic nerve hypoplasia (Fig. 18.59a and b), this involves a spectrum of midline developmental brain defects which may or may not be associated with endocrine abnormalities. These defects include absence or dysgenesis of the septum pellucidum (Fig. 18.59c), thinning or agenesis of the corpus callosum (Fig. 18.60), dysplasia of the anterior third ventricle. Hypopituitarism with low growth hormone levels is common and if recognized early, the deficiency can be corrected and normal growth resumed. It has been suggested that retinal venous tortuosity in patients with bilateral optic nerve hypoplasia may be a marker for potential endocrine dysfunction.
2. **Frontonasal dysplasia** (*see* above) is an occasional association.

Aicardi syndrome

Aicardi syndrome is a very rare X-linked dominant disorder which is lethal *in utero* for males. Ocular involvement is usually bilateral but often asymmetrical.

1. **Signs**
   - Multiple depigmented 'chorioretinal lacunae' clustered around the disc are pathognomonic (Fig. 18.61).
   - Congenital disc anomalies include coloboma, hypoplasia and pigmentation.
2. **Other ocular features** include microphthalmos, persistent pupillary membranes, cataract and iris colobomas.
3. **Systemic features** include infantile spasms, agenesis of the corpus callosum, skeletal malformations and psycho-

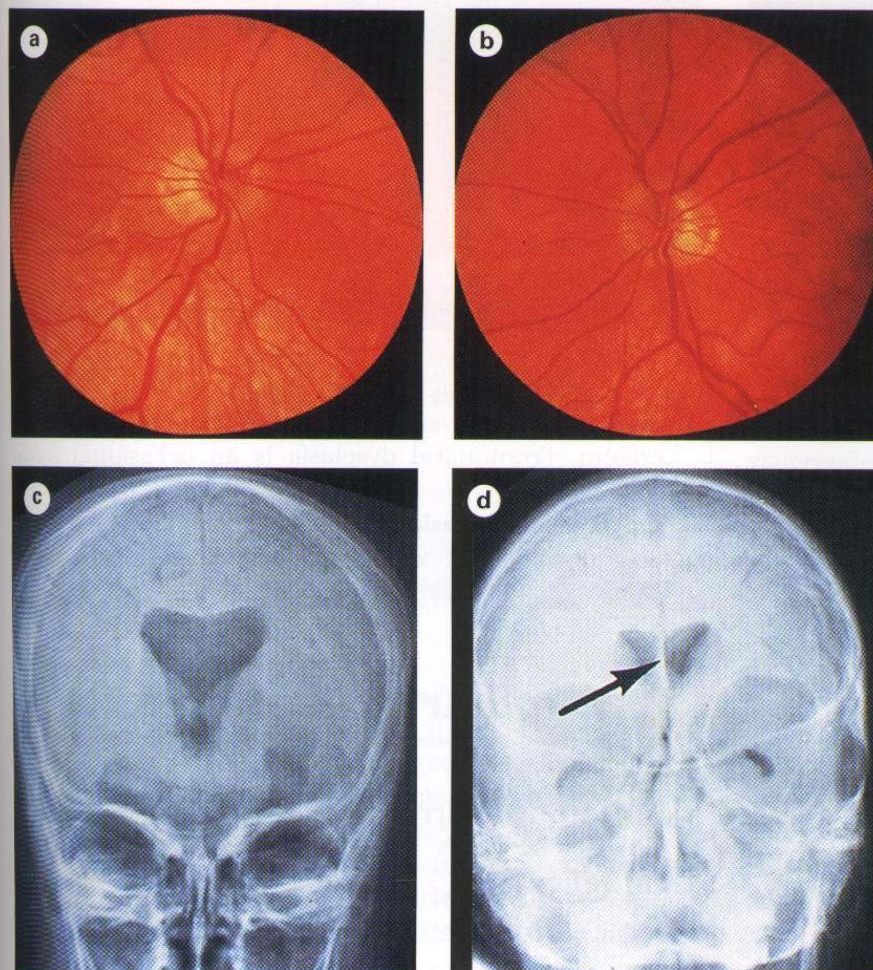
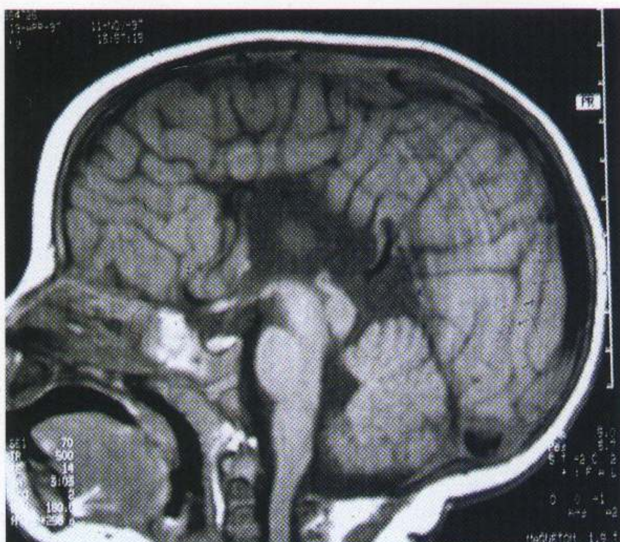
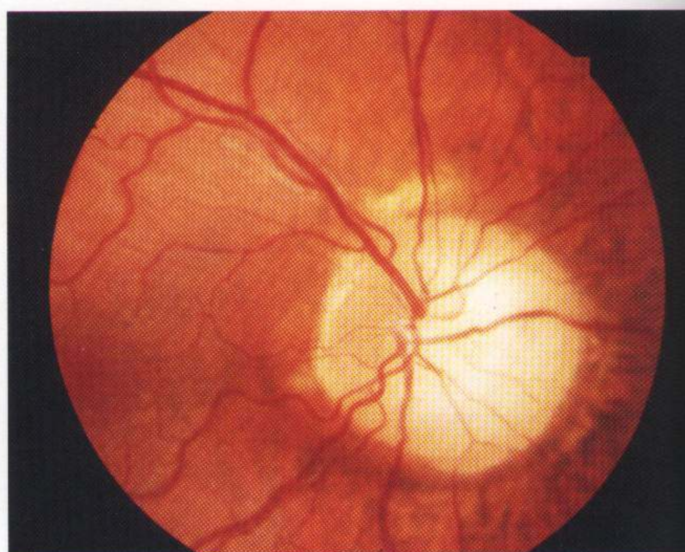
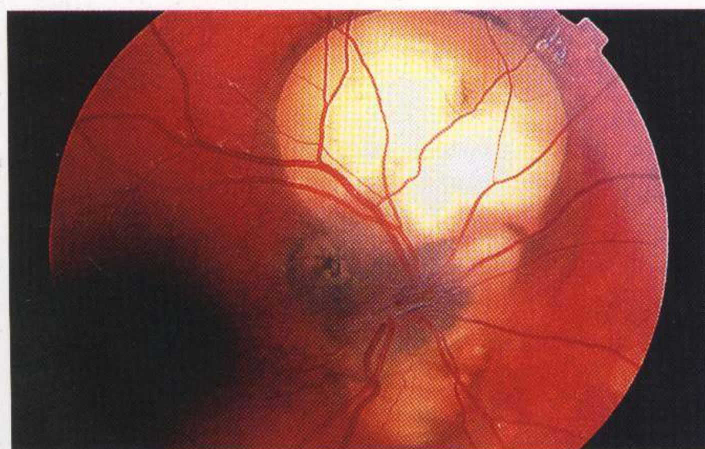
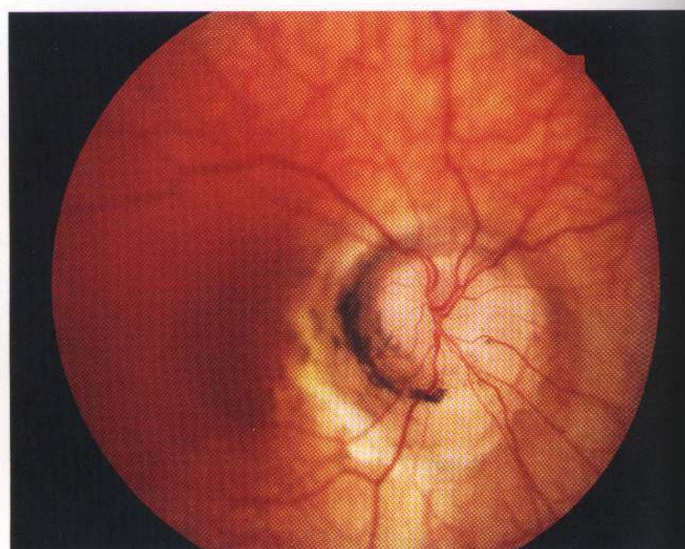


Fig. 18.59
de Morsier syndrome. (**a** and **b**) Optic disc hypoplasia; (**c**) absence of the septum pellucidum; (**d**) normal septum pellucidum (arrow) for comparison (Courtesy of Wilmer Institute)


Fig. 18.60
Sagittal MRI scan showing absence of the corpus callosum
(Courtesy of K. Nischal)


Fig. 18.62
Megalopapilla


Fig. 18.61
Anomalous optic disc and chorioretinal lacunae in Aicardi syndrome


Fig. 18.63
Parapapillary staphyloma

motor retardation. Other serious CNS malformations may also be present and death usually occurs within the first few years of life.

Other anomalies

Miscellaneous rare optic disc anomalies which occasionally have neurological associations include the following:

1. **Megalopapilla**, in which the horizontal and vertical disc diameters are 2.1 mm or more (Fig. 18.62).
2. **Parapapillary staphyloma** is a non-hereditary, usually unilateral condition in which a relatively normal disc sits at the base of a deep excavation whose walls, as well as the surrounding choroid and retinal pigment epithelium, show atrophic changes (Fig. 18.63). Visual acuity is markedly reduced and local retinal detachment may be present. Frontonasal dysplasia is an occasional association.
3. **Optic disc dysplasia** is a descriptive term for a markedly deformed disc that does not conform to any recognizable category (Fig. 18.64).

Pupillary reactions

Applied anatomy

Light reflex

The light reflex is mediated by the retinal photoreceptors and subserved by four neurones (Fig. 18.65).

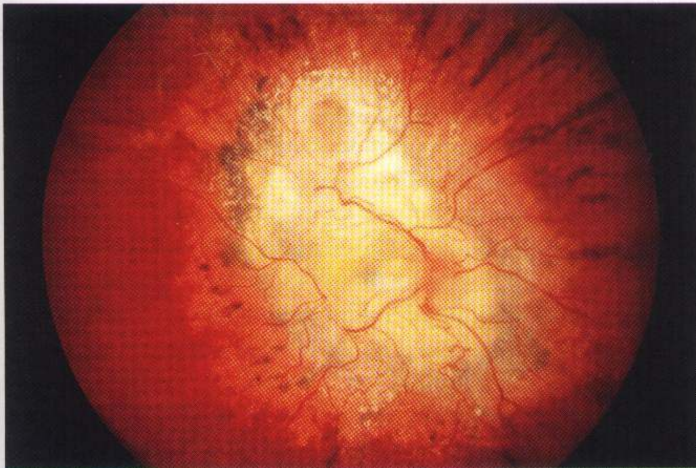


Fig. 18.64
Dysplastic disc (Courtesy of C. Barry)

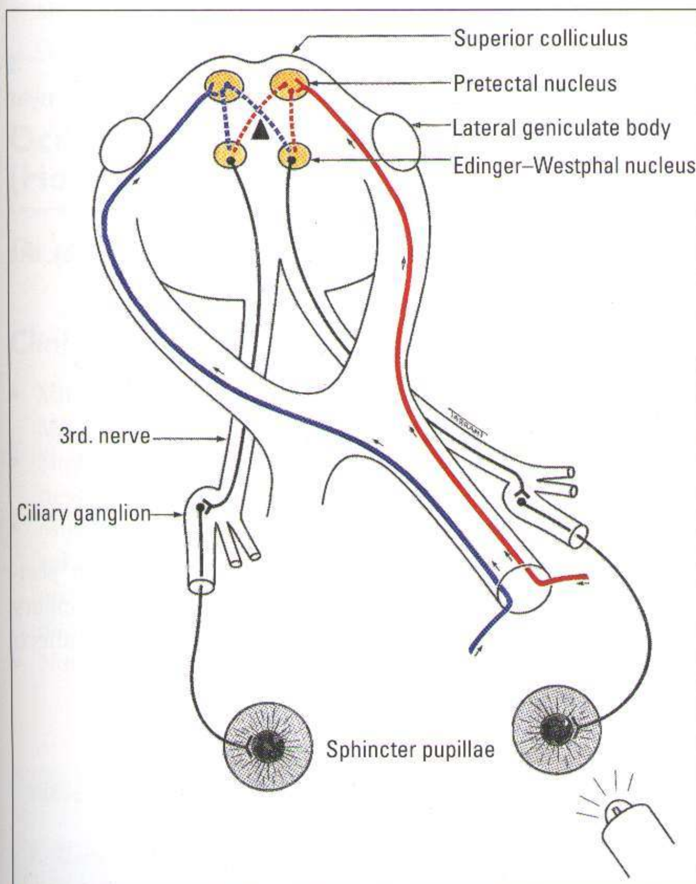


Fig. 18.65
Anatomical pathway of the pupillary light reflex

1. **The first** (sensory) connects each retina with both pretectal nuclei in the midbrain at the level of the superior colliculi. Impulses originating from the nasal retina are conducted by fibres which decussate in the chiasm and pass up the opposite optic tract to terminate in the contralateral pretectal nucleus. Impulses originating in the temporal retina are conducted by uncrossed fibres (ipsilateral optic tract) which terminate in the ipsilateral pretectal nucleus.
2. **The second** (internuncial) connects each pretectal nucleus to both Edinger–Westphal nuclei. Thus a uniocular light stimulus evokes bilateral and symmetrical pupillary constriction. Damage to these internuncial neurones is responsible for light-near dissociation in neurosyphilis and pinealomas.
3. **The third** (preganglionic motor) connects the Edinger–Westphal nucleus to the ciliary ganglion. The parasympathetic fibres pass through the oculomotor nerve, enter its inferior division and reach the ciliary ganglion via the nerve to the inferior oblique muscle.
4. **The fourth** (postganglionic motor) leaves the ciliary ganglion and passes in the short ciliary nerves to innervate the sphincter pupillae. The ciliary ganglion is located within the muscle cone, just behind the globe. It should be noted that, although the ciliary ganglion serves as a conduit for other nerve fibres, only the parasympathetic fibres synapse there.

Near reflex

The near reflex, a synkinesis rather than a true reflex, is activated when gaze is changed from a distant to a near target. It comprises accommodation, convergence and miosis. Vision is not a prerequisite for the near reflex, and there is no clinical condition in which the light reflex is present but the near response absent. Although the final pathways for the near and light reflexes are identical (i.e. third nerve, ciliary ganglion, short ciliary nerves), the centre for the near reflex is ill-defined. There are probably two supranuclear influences: the frontal and occipital lobes. The midbrain centre for the near reflex is probably located more ventrally than the pretectal nucleus and this may explain why compressive lesions such as pinealomas preferentially involve the dorsal internuncial neurones involved in the light reflex, sparing the ventral (near reflex) fibres until later.

Sympathetic innervation

The sympathetic supply involves three neurones (Fig. 18.66):

1. **The first** (central) starts in the posterior hypothalamus and descends, uncrossed, down the brain stem to terminate in the ciliospinal centre of Budge, in the intermediolateral horn of the spinal cord, located between C8 and T2.
2. **The second** (preganglionic) passes from the ciliospinal centre to the superior cervical ganglion in the neck. During its long course, it is closely related to the apical pleura, where it may be damaged by bronchogenic carcinoma (Pancoast tumour) or during surgery on the neck.
3. **The third** (postganglionic) ascends along the internal carotid artery to enter the cavernous sinus where it joins the ophthalmic division of the trigeminal nerve. The sympathetic fibres reach the ciliary body and the dilator pupillae muscle via the nasociliary nerve and the long ciliary nerves.

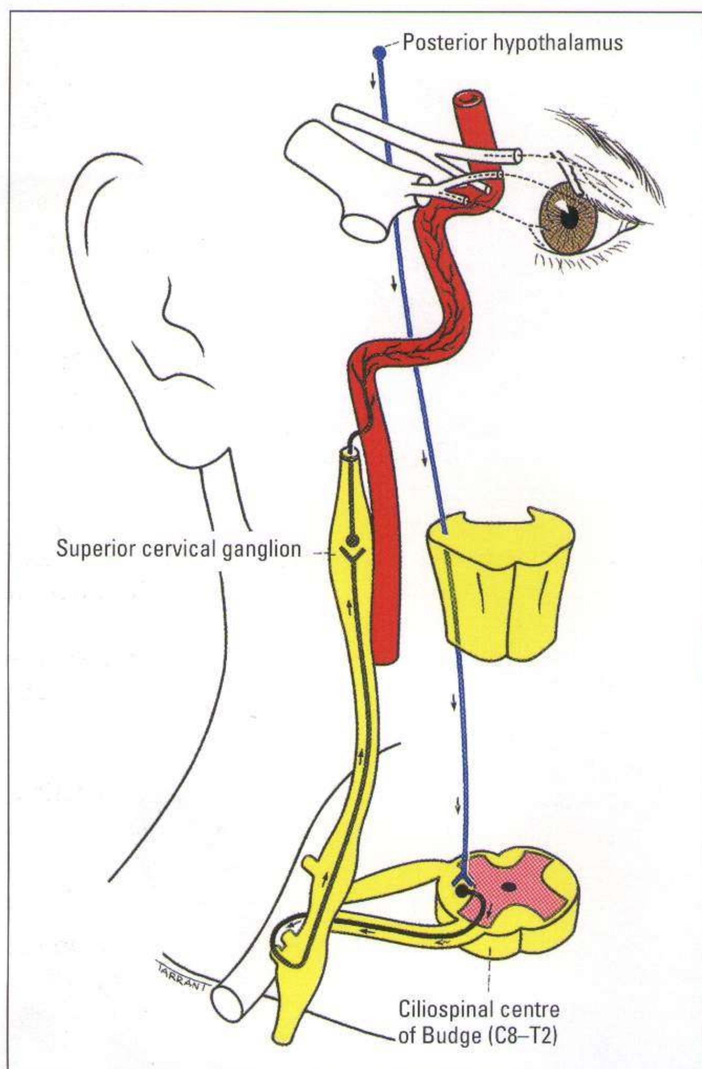


Fig. 18.66
Anatomical pathway of the sympathetic nerve supply

Afferent pupillary defects

Absolute afferent pupillary defect

An absolute afferent pupillary defect (amaurotic pupil) is caused by a complete optic nerve lesion and is characterized by the following:

- The involved eye is completely blind (i.e. no light perception).
- Both pupils are equal in size.
- When the affected eye is stimulated by light neither pupil reacts but when the normal eye is stimulated both pupils react normally.
- The near reflex is normal in both eyes.

Relative afferent pupillary defect

A relative pupillary defect (Marcus Gunn pupil) is caused by an incomplete optic nerve lesion or severe retinal disease, but never by a dense cataract. The clinical features are those of an amaurotic pupil but more subtle. Thus the pupils respond weakly to stimulation of the diseased eye and briskly to that of the normal eye. The difference between the pupillary reactions of the two eyes is highlighted by the '*swinging-flashlight test*' in which a light source is alternatively switched from one eye to the other and back, thus stimulating each eye in rapid succession. First the normal eye is stimulated, resulting in brisk constriction of both pupils. Then when the light is swung to the diseased eye, both pupils dilate instead of constricting. This paradoxical dilatation of the pupils in response to light occurs because the dilatation produced by withdrawing the light from the normal eye outweighs the constriction produced by stimulating the abnormal eye.

> ***NB:*** In afferent (sensory) lesions, the pupils are equal in size. Anisocoria (inequality of pupillary size) implies disease of the efferent (motor) nerve, iris or muscles of the pupil.

Light-near dissociation

Here the light reflex is absent or sluggish but the near response is normal. The causes are shown in Table 18.1.

Argyll Robertson pupil

This is caused by neurosyphilis and is characterized by the following:

- Involvement is usually bilateral but asymmetrical.
- The pupils are small and irregular.
- Light-near dissociation.
- The pupils are very difficult to dilate.

Adie pupil

Adie (tonic) pupil is caused by denervation of the post-ganglionic supply to the sphincter pupillae and the ciliary muscle, which may follow a viral illness. It typically affects young adults and is unilateral in 80% of cases.

1. Signs
- Large and regular pupil.

Table 18.1 Causes of light-near dissociation

1. Unilateral
- afferent conduction defect
- Adie pupil
- herpes zoster ophthalmicus
- aberrant regeneration of third nerve

2. Bilateral
- neurosyphilis
- type 1 diabetes
- myotonic dystrophy
- Parinaud dorsal midbrain syndrome
- familial amyloidosis
- encephalitis
- chronic alcoholism

- Light reflex is absent or sluggish and is associated with vermiform movements of the pupillary border, visible on the slit-lamp.
- The pupil responds slowly in the near reflex, following which redilatation is slow.
- Accommodation may manifest similar tonicity, in that once a near object has been fixated the time taken to refocus in the distance (relax the ciliary muscle) is prolonged.
- In long-standing cases the pupil may become small ('little old Adie').

2. **Associations**, in some cases, are diminished deep tendon reflexes (Holmes–Adie syndrome) and autonomic nerve dysfunction.
3. **Pharmacological testing**. If 2.5% mecholyl or 0.125% pilocarpine is instilled into both eyes, the normal pupil will not constrict, but the abnormal pupil will because of denervation hypersensitivity. Some diabetic patients may also show this response and very occasionally both pupils constrict in normal individuals.

Oculosympathetic palsy (Horner syndrome)

The causes of Horner syndrome are shown in Table 18.2.

Clinical features

- Mild ptosis (usually 1–2 mm) as a result of weakness of Müller muscle (Fig. 18.67).
- Slight elevation of the inferior eyelid as a result of weakness of the inferior tarsal muscle.
- Miosis resulting from the unopposed action of the sphincter pupillae, with resultant anisocoria which is accentuated in dim light, since the Horner pupil will not dilate, like its fellow.
- Normal reactions to light and near.

Table 18.2 Causes of Horner syndrome

1. **Central (first-order neurone)**
   - brain stem disease (tumours, vascular, demyelination)
   - syringomyelia
   - lateral medullary (Wallenberg) syndrome
   - spinal cord tumours
2. **Preganglionic (second-order neurone)**
   - Pancoast tumour
   - carotid and aortic aneurysms and dissection
   - neck lesions (glands, trauma, postsurgical)
3. **Postganglionic (third-order neurone)**
   - cluster headaches (migrainous neuralgia)
   - internal carotid artery dissection
   - nasopharyngeal tumours
   - otitis media
   - cavernous sinus mass



Fig. 18.67
Right Horner syndrome

- Reduced ipsilateral sweating, but only if the lesion is below the superior cervical ganglion because the fibres supplying the skin of the face run along the external carotid artery.
- Hypochromic heterochromia (irides of different colour—Horner is lighter) may be seen if the lesion is congenital or long-standing.
- The pupil is slow to dilate.
- Less important signs include hyperactive accommodation, ocular hypotony and conjunctival hyperaemia.

Pharmacological tests

Cocaine confirms the diagnosis. Hydroxyamphetamine (Paredrine) may be used to differentiate a preganglionic from a postganglionic lesion. Adrenaline may also be used to assess denervation supersensitivity.

1. **Cocaine 4%** is instilled into both eyes.
   - *Result*: the normal pupil will dilate but the Horner pupil will not.
   - *Rationale*: noradrenaline (NA) released at the postganglionic sympathetic nerve endings is reuptaken by the nerve endings, thus terminating its action. Cocaine blocks this uptake. NA therefore accumulates and causes pupillary dilatation. In Horner syndrome, there is no NA being secreted in the first place; therefore cocaine has no effect. Cocaine thus confirms the diagnosis of Horner sydrome.
2. **Hydroxyamphetamine 1%** is instilled into both eyes.
   - *Result*: in a preganglionic lesion both pupils will dilate (Fig. 18.68) whereas in a postganglionic lesion the Horner pupil will not. (This needs to be performed the following day, after the effects of cocaine have worn off.)
   - *Rationale*: hydroxyamphetamine potentiates the release of NA from postganglionic nerve endings. If this neurone is intact (a lesion of the first- or second-order neurone, and also the normal eye) NA will be released and the pupil will dilate. In a lesion of the third-order (postganglionic) neurone there can be no dilatation since the neurone is destroyed.
3. **Adrenaline 1:1000** is instilled into both eyes.
   - *Result*: in a preganglionic lesion neither pupil will dilate because adrenaline is rapidly destroyed by monoamine



Fig. 18.68
(a) Right preganglionic Horner syndrome; **(b)** bilateral mydriasis following instillation of hydroxyamphetamine into both eyes

oxidase; in a postganglionic lesion, the Horner pupil will dilate and ptosis may be temporarily relieved because adrenaline is not broken down due to the absence of monoamine oxidase.

- *Rationale*: a muscle deprived of its motor supply manifests heightened sensitivity to the excitatory neurotransmitter secreted by its motor nerve. In Horner syndrome the dilator pupillae muscle similarly manifests 'denervation hypersensitivity' to adrenergic neurotransmitters. Therefore adrenaline, even in minute concentrations, produces marked dilatation of the Horner pupil.

Nystagmus

Introduction

Physiological principles

Nystagmus is a repetitive, involuntary, to-and-fro oscillation of the eyes, which may be physiological or pathological. Thus nystagmus that occurs in response to rotation of an optokinetic drum or of the body in space is normal and acts to preserve clear vision. Ocular movements that bring about fixation on an object of interest are called foveating and those that move the fovea away from the object are defoveating. In pathological nystagmus, each cycle of movement is usually initiated by an involuntary, defoveating drift of the eye away from the object of interest, followed by a returning refixational saccadic movement. The plane of nystagmus may be horizontal, vertical, torsional or non-specific. The amplitude of nystagmus refers to how far the eyes move, while the frequency refers to how often the eyes oscillate. On the basis of amplitude, nystagmus may be fine or coarse, while the frequency may be high, moderate or low.

Classification

1. **Jerk nystagmus** is saccadic with a slow defoveating 'drift' movement and a fast corrective refoveating saccadic movement. The direction of nystagmus is described in terms of the direction of the fast component, so that jerk nystagmus may be right, left, up, down or rotatory. Jerk nystagmus can be divided into gaze-evoked (i.e. vestibular) and gaze-paretic, which is slow and usually indicates brain stem damage.
2. **Pendular nystagmus** is non-saccadic in that both the foveating and defoveating movements are slow (i.e. the velocity of nystagmus is equal in both directions).
   - Congenital pendular nystagmus is horizontal, conjugate and tends to convert to jerk on lateral gaze.
   - Acquired pendular nystagmus has horizontal, vertical and torsional components.
   - If the horizontal and vertical components of pendular nystagmus are in phase (i.e. occur simultaneously) the perceived direction becomes oblique.
   - If the horizontal and vertical components are out of phase the direction becomes elliptic or rotatory.
3. **Mixed nystagmus** involves pendular nystagmus in the primary position and jerk nystagmus on lateral gaze.

The characteristics of any form of nystagmus can be documented using the scheme shown in Fig. 18.69.

Physiological nystagmus

1. **End-point nystagmus** is a fine jerk nystagmus of moderate frequency found when the eyes are in extreme positions of gaze. The fast phase is in the direction of gaze.
2. **Optokinetic nystagmus** is a jerk nystagmus induced by moving repetitive targets across the visual field. The slow phase is a pursuit movement in which the eyes follow the target; the fast phase is a saccadic movement in the opposite direction as the eyes fixate on the next target. If the optokinetic tape or drum is moved from right to left, the left parieto-occipital region controls the slow (pursuit) phase to the left, and the left frontal lobe controls the rapid (saccadic) phase to the right. Optokinetic nystagmus is useful for detecting malingerers who feign blindness and for testing visual acuity in the very young. It may also be helpful in determining the cause of an isolated homonymous hemianopia (*see* below).
3. **Vestibular nystagmus** is a jerk nystagmus caused by altered input from the vestibular nuclei to the horizontal gaze centres. The slow phase is initiated by the vestibular nuclei and the fast phase by the brain stem and fronto-mesencephalic pathway. Rotatory nystagmus is usually caused by pathological conditions affecting the vestibular system. Vestibular nystagmus may be elicited by caloric stimulation as follows:
   - When *cold* water is poured into the *right ear* the patient will develop *left* jerk nystagmus (i.e. fast phase to the left).

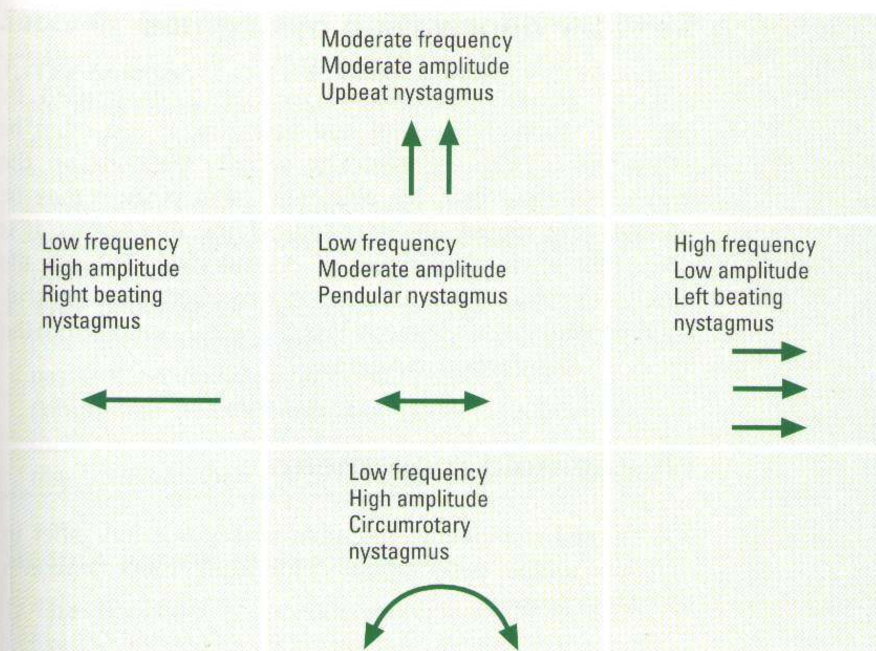


Fig. 18.69
Scheme for documenting nystagmus (Courtesy of J. Ferris)

- When *warm* water is poured into the *right ear* the patient will develop *right* jerk nystagmus (i.e. fast phase to the right). A useful mnemonic is '*COWS*' (cold–opposite, warm–same) indicating the direction of the nystagmus.
- When cold water is poured into both ears simultaneously, a jerk nystagmus with the fast phase upwards develops; warm water in both ears elicits nystagmus with the fast phase downwards (cold 'slows things down').

Motor imbalance nystagmus

Motor imbalance nystagmus is the result of primary defects in the efferent mechanisms.

Congenital nystagmus

1. **Inheritance** may be XL recessive or AD.
2. **Presentation** is about 2–3 months after birth and persists throughout life.
3. **Signs**
   - Uniplanar horizontal nystagmus, usually of the jerk type.
   - It may be dampened by convergence and is not present during sleep.
   - There is usually a null point: a position of gaze in which nystagmus is minimal.
   - In order to move the eyes into the null point, an abnormal head posture may be adopted.

Spasmas nutans

1. **Presentation** of this rare condition is between 3 and 18 months.
2. **Signs**
   - Unilateral or bilateral, small-amplitude, high-frequency horizontal nystagmus associated with head nodding.
   - It is frequently asymmetrical with increased amplitude in abduction.
   - Vertical and torsional components may be present.
3. **Causes**
   - Idiopathic which spontaneously resolves by age 3 years.
   - Glioma of anterior visual pathway, empty sella syndrome and porencephalic cyst.

Latent nystagmus

This is associated with infantile esotropia and dissociated vertical deviation (*see* Chapter 16). It is characterized by the following:

- With both eyes open there is no nystagmus.
- Horizontal nystagmus, becomes apparent on covering one eye or reducing the amount of light reaching the eye.
- Fast phase is in the direction of the uncovered fixating eye.
- Occasionally, an element of latency may be superimposed on a manifest nystagmus so that when one eye is covered the amplitude of nystagmus increases (latent-manifest nystagmus).

Periodic alternating nystagmus

1. **Signs**
   - Conjugate horizontal jerk nystagmus that periodically reverses its direction.
   - Each cycle may be divided into active and quiescent phases as follows.
   - During the active phase, the amplitude, frequency and slow-phase velocity of nystagmus first progressively increase, then decrease.

- This is followed by a short, quiet interlude, lasting 4–20 seconds, during which time the eyes are steady and show low-intensity, often pendular movements.
- A similar sequence in the opposite direction occurs thereafter, the whole cycle lasting between 1 and 3 minutes.

2. **Causes** include cerebellar disease, demyelination, ataxia telangiectasia (Louis–Bar syndrome) and drugs such as phenytoin.

Convergence–retraction nystagmus

This is caused by co-contraction of the extraocular muscles, particularly the medial recti.

1. **Signs**
   - Jerk nystagmus is induced by passing an OKN tape downwards.
   - The upward refixation saccade brings the two eyes towards each other in a convergence movement.
   - Associated with retraction of the globe into the orbit.
2. **Causes** include lesions of the pretectal area such as pinealomas and vascular accidents.

Downbeat nystagmus

1. **Signs**. Vertical nystagmus with the fast phase beating downwards, which is more easily elicited in downgaze.
2. **Causes**
   - Lesions of the craniocervical junction at the foramen magnum such as an Arnold–Chiari malformation and syringobulbia.
   - Drugs such as lithium, phenytoin, carbamazepine and barbiturates.
   - Wernicke encephalopathy, demyelination and hydrocephalus.

Upbeat nystagmus

1. **Signs**. Vertical nystagmus with the fast phase beating upwards.
2. **Causes** include posterior fossa lesions, drugs and Wernicke encephalopathy.

See-saw nystagmus of Maddox

1. **Signs**. Pendular nystagmus, in which one eye elevates and intorts while the other depresses and extorts; the eyes then reverse direction.
2. **Causes** include parasellar tumours often producing bitemporal hemianopia, syringobulbia and brain stem stroke.

Ataxic nystagmus

This is a horizontal jerk nystagmus which occurs in the abducting eye of a patient with an internuclear ophthalmoplegia (*see* later).

Sensory deprivation nystagmus

Sensory deprivation (ocular) nystagmus is caused by defective vision. Horizontal and pendular, it can often be dampened by convergence. The severity depends on the degree of visual loss. An abnormal head posture may be adopted to decrease the amplitude of the nystagmus. It is caused by severe impairment of central vision in early life (e.g. congenital cataract, macular hypoplasia). In general, children who sustain bilateral loss of central vision before the age of 2 years develop nystagmus.

Nystagmoid movements

Nystagmoid movements resemble nystagmus but differ in that the initial, pathological defoveating movement is a saccadic intrusion.

Ocular flutter and opsoclonus

1. **Signs**
   - Saccadic oscillations with no intersaccadic interval.
   - In ocular flutter they are purely horizontal and in opsoclonus they are multiplanar.
2. **Causes** include viral encephalitis, myoclonic encephalopathy in infants ('dancing eyes and dancing feet'), transient (idiopathic) in healthy neonates and drug-induced (lithium, amitriptyline and phenytoin).

Ocular bobbing

1. **Signs**. Rapid, conjugate, downward eye movements with a slow drift up to the primary position.
2. **Causes** include pontine lesions (usually haemorrhage), cerebellar lesions compressing the pons and metabolic encephalopathy.

Supranuclear disorders of ocular motility

Conjugate eye movements

Conjugate eye movements or 'versions' are binocular movements in which the eyes move synchronously and symmetrically in the same direction. The three main types are: (a) *saccadic*, (b) *smooth pursuit* and (c) *non-optical reflex*. Saccadic and pursuit movements are controlled at both cerebral and brain stem levels. Supranuclear disturbances produce gaze palsies, characterized by absence of diplopia and normal vestibulo-ocular reflexes (e.g. oculocephalic movements and caloric stimulation).

Saccadic movements

1. **The function** of saccadic (fixating) movements is to place the object of interest on to the fovea rapidly or to move the eyes from one object to another. This can be done voluntarily or reflexly, triggered by the presence of an object in the peripheral visual field. Voluntary saccades are similar to the gunnery system of rapidly locating a moving target.
2. **The pathway** for horizontal saccades originates in the premotor cortex (the frontal eye fields). From there, fibres pass to the *contralateral* horizontal gaze centre in the pontine paramedian reticular formation (PPRF). Each frontal lobe therefore initiates contralateral saccades. Irritative lesions may therefore cause ocular deviation to the opposite side.

Smooth pursuit movements

1. **The function** of pursuit movements is to maintain fixation on a target once it has been located by the saccadic system. The stimulus is movement of the image near the fovea. The movements are slow and smooth.
2. **The pathway** originates in the peristriate cortex of the occipital lobe. The fibres descend and terminate in the *ipsilateral* horizontal gaze centre in the PPRF. Each occipital lobe therefore controls pursuit to the ipsilateral side.

Non-optical reflexes

1. **The function** of non-optical (vestibular) reflexes is to maintain eye position with respect to any changes of head and body position.
2. **The pathway** originates in the labyrinths and proprioceptors in the neck muscles which mediate information concerning head and neck movements. Afferent fibres synapse in the vestibular nuclei and pass to the horizontal gaze centre in the PPRF.

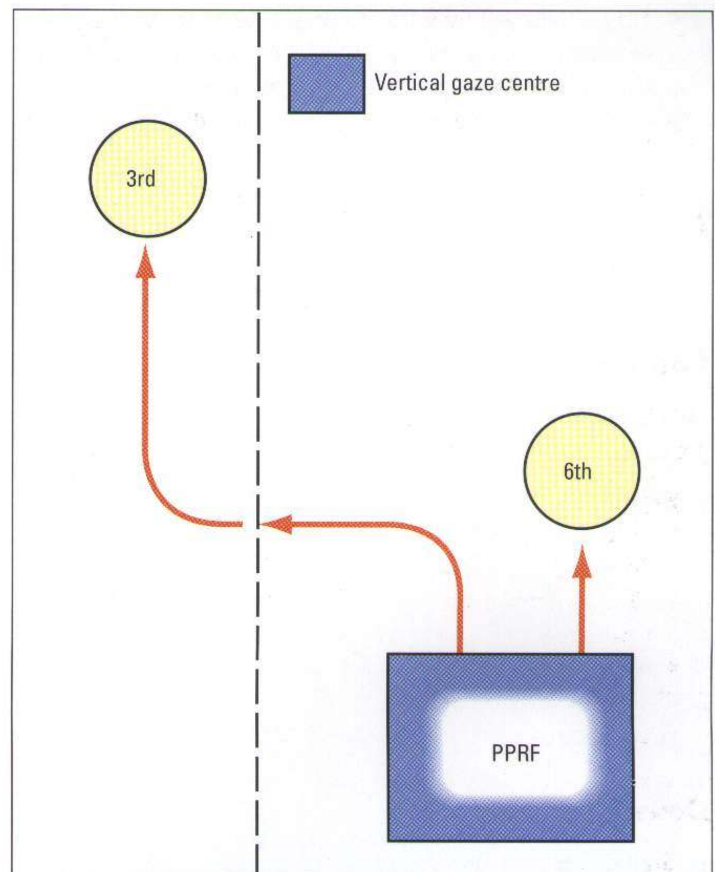


Fig. 18.70
Anatomical pathways for horizontal eye movements

Horizontal gaze palsies

Applied anatomy

Horizontal eye movements are generated from the horizontal gaze centre in the PPRF (Fig. 18.70). From here fibres connect to the ipsilateral sixth nerve nucleus to abduct the ipsilateral eye. To adduct the contralateral eye, fibres from the PPRF also cross the midline at the level of the pons and pass up the contralateral medial longitudinal fasciculus (MLF) to the medial rectus subnucleus in the contralateral third nerve complex (which also receives independent descending input from the vergence control centres). Stimulation of the PPRF on one side therefore causes a conjugate movement of the eyes to the same side. It is important to remember that once the MLF leaves the PPRF, it crosses the midline immediately, and then ascends on the contralateral side. Loss of normal horizontal eye movements occurs when these pathways are disrupted. The causes are shown in Table 18.3.

Table 18.3 Causes of internuclear ophthalmoplegia
• demyelination
• vascular disease
• tumours of the brain stem and fourth ventricle
• trauma
• encephalitis
• hydrocephalus
• progressive supranuclear palsy
• drug-induced
• remote effects of carcinoma

Signs

1. **A PPRF** lesion gives rise to an ipsilateral horizontal gaze palsy (inability to look in the direction of the lesion).
2. **A MLF** lesion is responsible for the clinical syndrome of internuclear ophthalmoplegia (INO). A left internuclear ophthalmoplegia is characterized by the following:
   - On right gaze there is defective left adduction and ataxic nystagmus of the right eye (Fig. 18.71a).
   - Left gaze is normal (Fig. 18.71b).
   - Convergence is intact if the lesion is discrete.
   - Vertical nystagmus on attempted upgaze.



Fig. 18.71
Left internuclear ophthalmoplegia. (**a**) Defective left adduction on right gaze; (**b**) normal left gaze

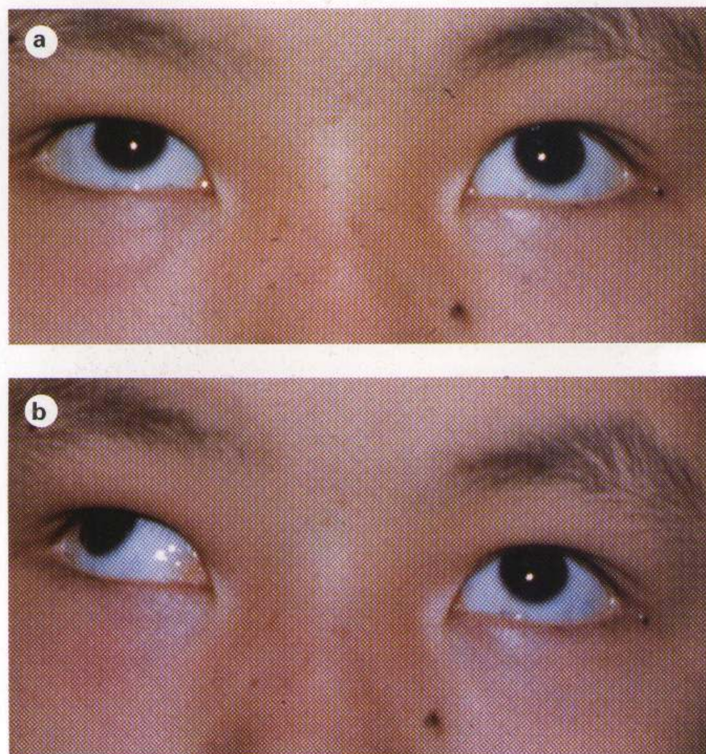


Fig. 18.72
Left 'one-and-a-half syndrome'. (**a**) Defective left gaze; (**b**) defective left adduction and normal right abduction on right gaze (Courtesy of K. Nischal)

3. **PPRF** and **MLF** combined lesions on the same side give rise to the 'one-and-a-half syndrome'. A left lesion is characterized by:
   - Ipsilateral gaze palsy. Figure 18.72a shows the patient attempting left gaze.
   - Ipsilateral internuclear ophthalmoplegia. Figure 18.72b shows the patient attempting right gaze.
   - The only residual movement is abduction of the contralateral eye, which also exhibits ataxic nystagmus.

Vertical gaze palsies

Applied anatomy

Vertical eye movements are generated from the vertical gaze centre known as the rostral interstitial nucleus of the MLF, which lies in the midbrain just dorsal to the red nucleus. From the vertical gaze centre, impulses pass to the subnuclei of the eye muscles controlling vertical gaze in both eyes. Cells mediating upward and downward eye movements are intermingled in the vertical gaze centre, although selective paralysis of upgaze and downgaze may occur in spite of this.

Parinaud dorsal midbrain syndrome

1. **Signs**
   - Supranuclear upgaze palsy (Fig. 18.73a).
   - Straight eyes in the primary position (Fig. 18.73b)
   - Normal downgaze (Fig. 18.73c).
   - Large pupils with light-near dissociation.
   - Lid retraction (Collier sign).
   - Paralysis of convergence.
   - Convergence–retraction nystagmus.
2. **Causes**
   a. *In children*. Aqueduct stenosis, meningitis and pinealoma (Fig. 18.74).
   b. *In young adults*. Demyelination, trauma and arteriovenous malformations.
   c. *In the elderly*. Midbrain vascular accidents, mass lesions involving the periaqueductal grey matter and posterior fossa aneurysms.

Progressive supranuclear palsy

Progressive supranuclear palsy (Steele–Richardson–Olszewski syndrome) is a severe degenerative disease which presents in old age and is characterized by:

- Supranuclear gaze palsy, which initially primarily affects downgaze.
- As the disease progresses upgaze is also affected.
- Horizontal movements subsequently become impaired and eventually a global gaze palsy develops.
- Pseudobulbar palsy.
- Extrapyramidal rigidity, gait ataxia and dementia.

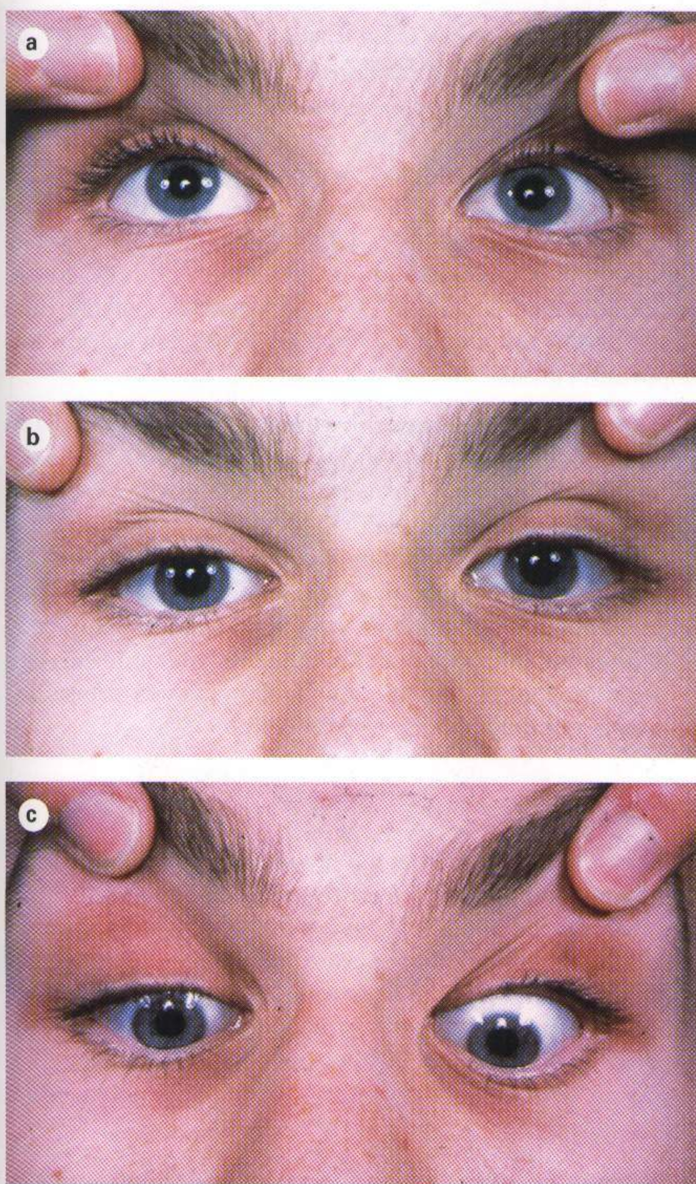
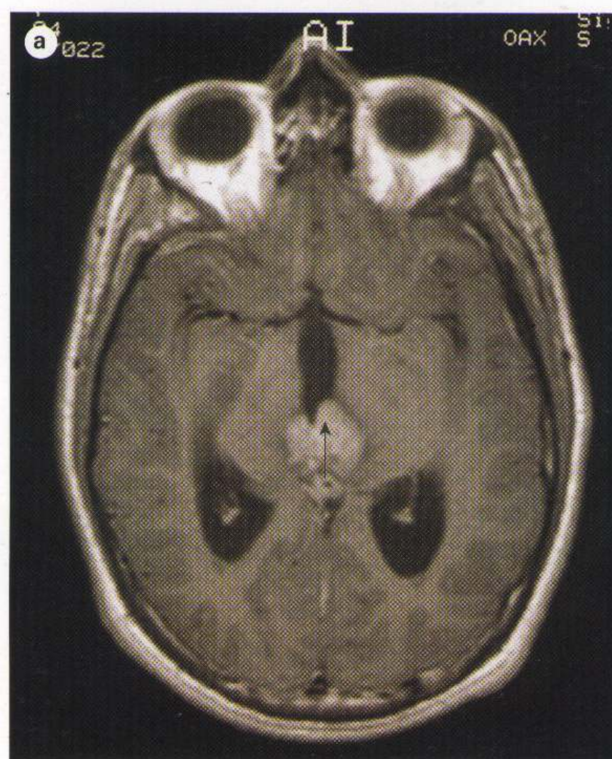


Fig. 18.73
Parinaud dorsal midbrain syndrome. (**a**) Defective upgaze; (**b**) straight eyes in primary position; (**c**) normal downgaze
(Courtesy of D. Thomas)



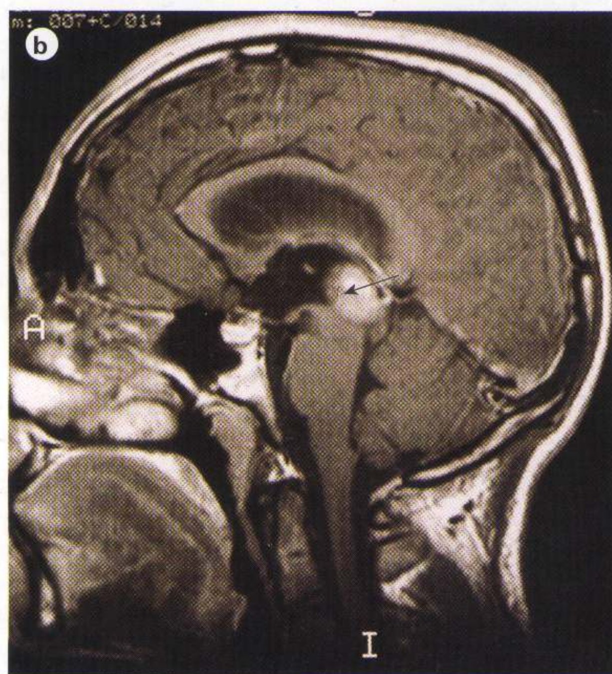


Fig. 18.74
T1-weighted MRI scan showing a pinealoma.
(**a**) axial view; (**b**) sagittal view—note dilated ventricles
(Courtesy of D. Thomas)

Third nerve

Applied anatomy

Nuclear complex

The nuclear complex of the third (oculomotor) nerve is situated in the midbrain at the level of the superior colliculus, ventral to the sylvian aqueduct (Fig. 18.75). It is composed of the following paired and unpaired subnuclei:

1. **Levator subnucleus** is an unpaired caudal midline structure which innervates both levator muscles. Lesions confined to this area will therefore give rise to bilateral ptosis.
2. **Superior rectus subnuclei** are paired; each innervates the respective contralateral superior rectus. A nuclear

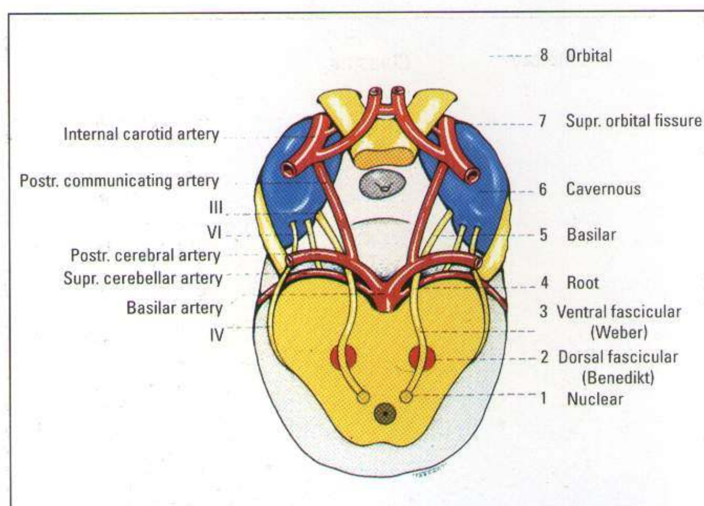


Fig. 18.75
Dorsal view of the course of the third nerve

third nerve palsy will spare the ipsilateral and affect the contralateral superior rectus.

3. **Medial rectus**, **inferior rectus** and **inferior oblique subnuclei** are paired and innervate their corresponding ipsilateral muscles. Lesions confined to the nuclear complex are relatively uncommon. The most frequent causes are vascular disease, primary tumours and metastases. Involvement of the paired medial rectus subnuclei causes a wall-eyed bilateral internuclear ophthalmoplegia (WEBINO), characterized by exotropia, and defective convergence and adduction. Lesions involving the entire nucleus are often associated with involvement of the adjacent and caudal fourth nerve nucleus.

Fasciculus

The fasciculus consists of efferent fibres which pass from the third nerve nucleus through the red nucleus and the medial aspect of the cerebral peduncle. They then emerge from the midbrain and pass into the interpeduncular space. The causes of nuclear and fascicular lesions are similar, except that demyelination may affect the fasciculus.

1. **Benedikt syndrome** involves the fasciculus as it passes through the red nucleus and is characterized by ipsilateral third nerve palsy and contralateral extrapyramidal signs such as hemitremor.
2. **Weber syndrome** involves the fasciculus as it passes through the cerebral peduncle and is characterized by an ipsilateral third nerve palsy and a contralateral hemiparesis.
3. **Nothnagel syndrome** involves the fasciculus and the superior cerebellar peduncle and is characterized by ipsilateral third nerve palsy and cerebellar ataxia. Important causes include vascular disease and tumours.
4. **Claude syndrome** is a combination of Benedikt and Nothnagel syndromes.

Basilar part

The basilar part starts as a series of 'rootlets' which leave the midbrain on the medial aspect of the cerebral peduncle, before coalescing to form the main trunk. The nerve then passes between the posterior cerebral and superior cerebellar arteries, running lateral to and parallel with the posterior communicating artery (Fig. 18.76). As the nerve traverses the base of the skull along its subarachnoid course unaccompanied by any other cranial nerve, isolated third nerve palsies are commonly basilar. The following are two important causes:

1. **Aneurysm** of the posterior communicating artery, at its junction with the internal carotid artery, (Fig. 18.77) typically presents as an acute, painful third nerve palsy with involvement of the pupil.
2. **Head trauma**, resulting in extradural or subdural haematoma, may cause a tentorial pressure cone with downward herniation of the temporal lobe. This compresses the third nerve as it passes over the tentorial edge, initially causing irritative miosis followed by mydriasis and a total third nerve palsy (Fig. 18.78).

Intracavernous part

The third nerve then enters the cavernous sinus by piercing the dura just lateral to the posterior clinoid process. Within the cavernous sinus, the third nerve runs in the lateral wall above the fourth nerve (Fig. 18.79). In the anterior part of the cavernous sinus, the nerve divides into superior and inferior branches which enter the orbit through the superior orbital fissure within the annulus of Zinn. The following are important causes of intracavernous third nerve palsies:

1. **Diabetes**, which may cause a vascular palsy, which usually spares the pupil.

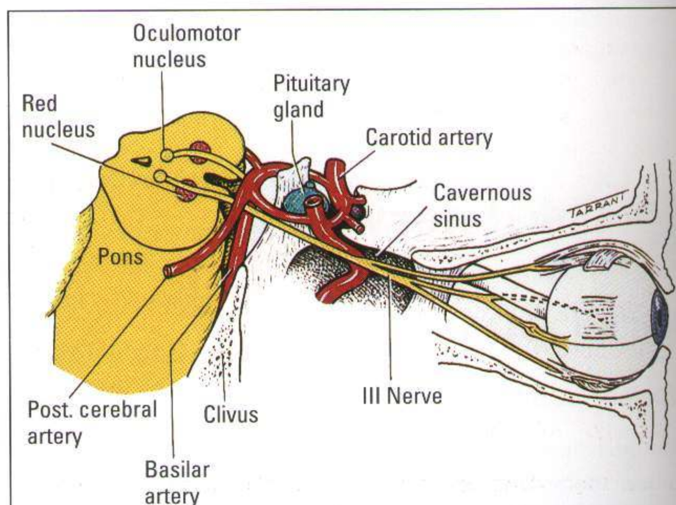


Fig. 18.76
Lateral view of the course of the third nerve

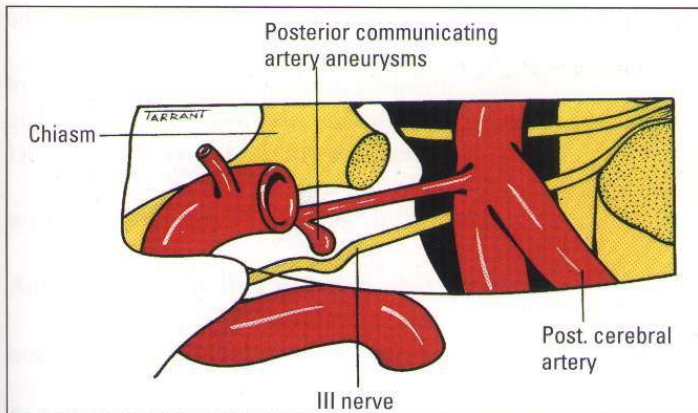


Fig. 18.77
Compression of the third nerve by a posterior communicating aneurysm

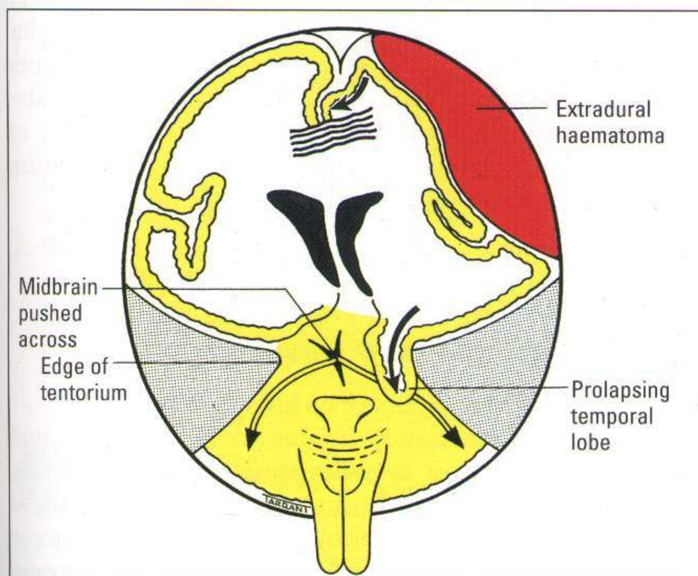


Fig. 18.78
Mechanism of third nerve palsy by extradural or subdural haematoma

2. **Pituitary apoplexy** (haemorrhagic infarction) may cause a third nerve palsy (e.g. after childbirth) if the gland swells laterally and impinges on the cavernous sinus.
3. **Intracavernous pathology** such as aneurysm, meningioma, carotid–cavernous fistula and granulomatous inflammation (Tolosa–Hunt syndrome) may all cause third nerve palsy. Because of its close proximity to other cranial nerves, intracavernous third nerve palsies are usually associated with involvement of the fourth and sixth nerves and the first division of the trigeminal nerve.

Intraorbital part

1. **Superior division** innervates the levator and superior rectus muscles.
2. **Inferior division** innervates the medial rectus, the inferior rectus and the inferior oblique muscles. The branch to the inferior oblique also contains preganglionic parasympathetic fibres from the Edinger–Westphal subnucleus, which innervate the sphincter pupillae and the ciliary muscle. Lesions of the inferior division are characterized by limited adduction and depression, and a dilated pupil. Both superior and inferior division palsies are commonly traumatic or vascular.

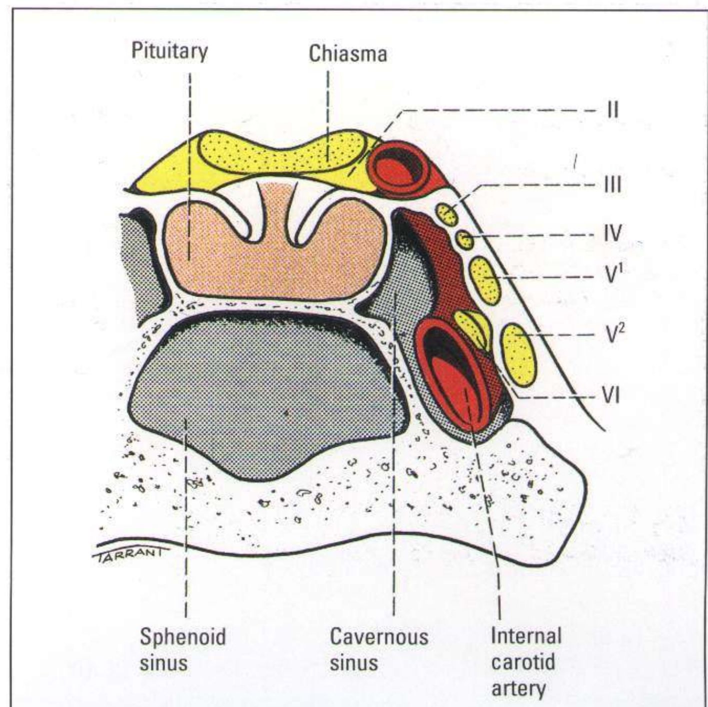


Fig. 18.79
Location of the cranial nerves in the cavernous sinus viewed from behind

Pupillomotor fibres

Between the brain stem and the cavernous sinus, the pupillomotor parasympathetic fibres are located superficially in the superomedial part of the third nerve (Fig. 18.80). They derive their blood supply from the pial blood vessels, whereas the main trunk of the third nerve is supplied by the vasa nervorum. Involvement or otherwise of the pupil is of great importance because it frequently differentiates a 'surgical' from a 'medical' lesion. Pupillary involvement, like other features of third nerve palsy, may be complete or partial, and may demonstrate features of recovery. Mild mydriasis and non-reactivity may therefore be clinically significant.

1. **Surgical lesions** such as aneurysms, trauma and uncal herniation characteristically involve the pupil by compressing the pial blood vessels and the superficially located pupillary fibres.
2. **Medical lesions** such as hypertension and diabetes usually spare the pupil. This is because the microangiopathy associated with medical lesions involves the vasa nervorum, causing ischaemia of the main trunk of the nerve, sparing the superficial pupillary fibres.

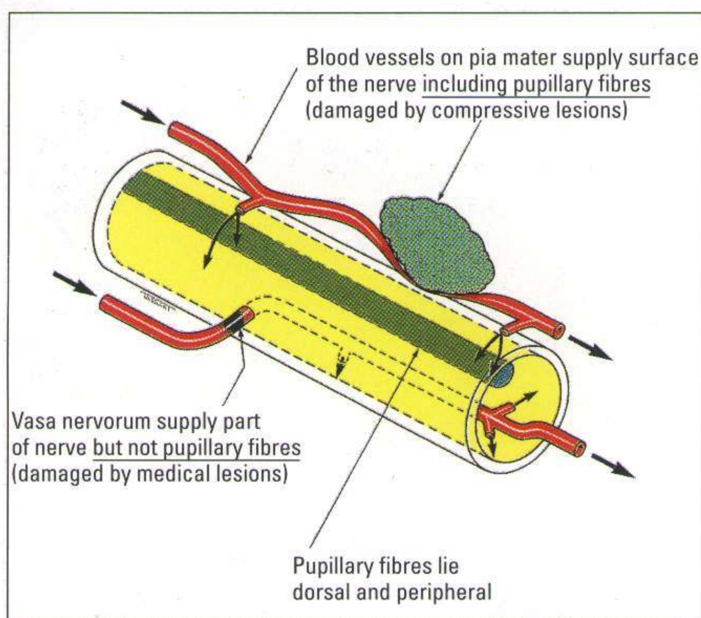


Fig. 18.80
Location of the pupillomotor fibres within the trunk of the third nerve

> *NB:* These principles are, however, not infallible; pupil involvement may be seen in some diabetic-associated third nerve palsies, while pupillary sparing does not invariably exclude an aneurysm or some other compressive lesion. Sometimes pupillary involvement may be the only sign of a third nerve palsy (basal meningitis, uncal herniation).

Clinical aspects

Clinical features

1. **Signs** of a left third nerve palsy (Fig. 18.81).
   - Weakness of the levator causing profound ptosis, due to which there is often no diplopia (Fig. 18.81a).
   - Unopposed action of lateral rectus causing the eye to be abducted in the primary position (Fig. 18.81b).
   - The intact superior oblique muscle causes intorsion of the eye at rest, which increases on attempted downgaze.
   - Normal abduction because the lateral rectus is intact (Fig. 18.81c).
   - Weakness of medial rectus limiting adduction (Fig. 18.81d).
   - Weakness of superior rectus and inferior oblique, limiting elevation (Fig. 18.81e).
   - Weakness of inferior rectus limiting depression (Fig. 18.81f).
   - Parasympathetic palsy causing a dilated pupil associated with defective accommodation.
2. **Aberrant regeneration** may follow acute traumatic and aneurysmal, but not vascular, third nerve palsies. This is because the endoneural nerve sheaths, which may be breached in traumatic and compressive lesions, remain intact in vascular pathology. Bizarre defects in ocular motility (*see* Fig. 1.123), such as elevation of the upper eyelid on attempted adduction or depression (the pseudo-Graefe phenomenon), are caused by misdirection of regenerating axons which reinnervate the wrong extraocular muscle. The pupil may also be involved.

Causes of isolated third nerve palsy

1. **Idiopathic**: about 25% have no known cause.
2. **Vascular disease**, such as due to hypertension and diabetes, is the most common cause of a pupil-sparing third nerve palsy. All patients should therefore have blood pressure measurement, urinalysis and plasma glucose estimation. In most cases spontaneous recovery occurs within 3 months. Diabetic third nerve palsy is often associated with periorbital pain and may occasionally be the presenting feature of diabetes. The presence of pain is therefore not helpful in differentiating aneurysmal and diabetic third nerve palsy.

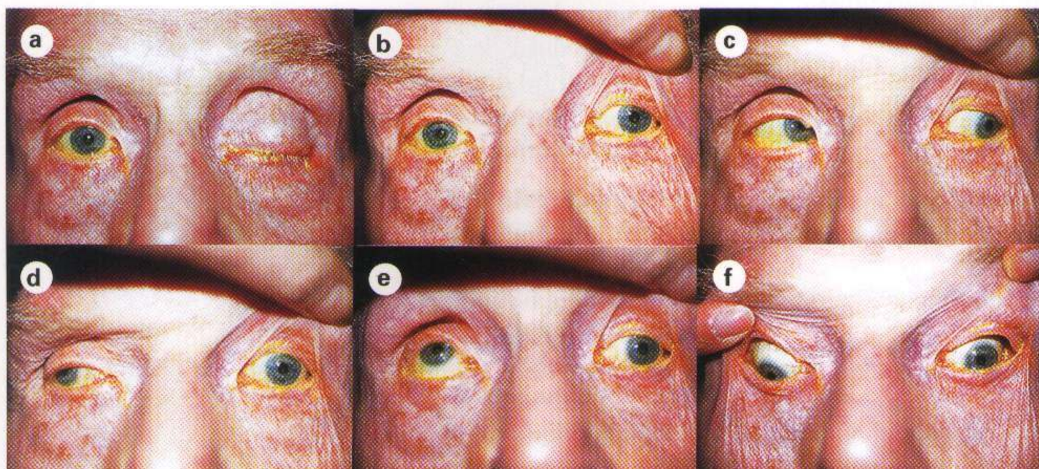


Fig. 18.81
Left third nerve palsy (*see text*)

3. **Trauma**, both direct and secondary to subdural haematoma with uncal herniation, is also a common cause. However, the development of third nerve palsy following relatively trivial head trauma, not associated with loss of consciousness, should alert the clinician to the possibility of an associated basal intracranial tumour which has caused the nerve trunk to be stretched and tethered.
4. **Aneurysm** of the posterior communicating artery at its junction with the internal carotid is a very important cause of an isolated painful third nerve palsy with involvement of the pupil.
5. **Miscellaneous** uncommon causes include tumours, syphilis and vasculitis associated with collagen vascular disorders.

Management

1. **Non-surgical** treatment options include the use of Fresnel prisms if the angle of deviation is small, uniocular occlusion to avoid diplopia (if ptosis is partial or recovering) and botulinum toxin injection into the uninvolved lateral rectus muscle to prevent its contracture before the deviation improves or stabilizes (*see* Chapter 16).
2. **Surgical** treatment, as with other ocular motor nerve palsies, should be contemplated only after all spontaneous improvement has ceased. This is usually not earlier than 6 months from the date of onset (*see* Chapter 16).

Fourth nerve

Applied anatomy

1. **Important features** of the fourth (trochlear) nerve are the following:
   - It is the only cranial nerve to emerge from the dorsal aspect of the brain.
   - It is a crossed cranial nerve; this means that the fourth nerve nucleus innervates the contralateral superior oblique muscle.
   - It is a very long and slender nerve.
2. **The nucleus** of the fourth nerve is located at the level of the inferior colliculi ventral to the sylvian aqueduct (Fig. 18.82). It is caudal to, and continuous with, the third nerve nuclear complex.
3. **The fasciculus** consists of axons which curve posteriorly around the aqueduct and decussate completely in the anterior medullary velum.
4. **The trunk** leaves the brain stem on the dorsal surface, just caudal to the inferior colliculus. It then curves laterally around the brain stem, runs forwards beneath the free edge of the tentorium, and (like the third nerve) passes between the posterior cerebral artery and the superior cerebellar artery. It then pierces the dura and enters the cavernous sinus.

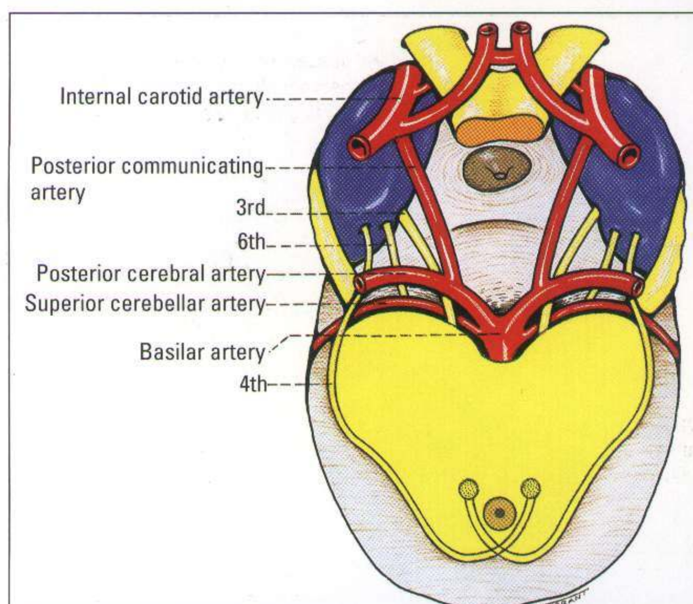


Fig. 18.82
Dorsal view of the course of the fourth nerve

5. **The intracavernous part** runs in the lateral wall of the sinus, inferiorly to the third nerve and above the first division of the fifth. In the anterior part of the cavernous sinus it rises and passes through the superior orbital fissure above and lateral to the annulus of Zinn.
6. **The intraorbital part** innervates the superior oblique muscle.

Clinical features

Acute onset of vertical diplopia in the absence of ptosis, combined with a characteristic head posture, strongly suggests fourth nerve disease. The features of nuclear, fascicular and peripheral fourth nerve palsies are clinically identical, except that nuclear palsies produce contralateral superior oblique weakness. A left fourth nerve palsy is illustrated.

1. **Signs**
   - Left limitation of depression in adduction due to superior oblique weakness (Fig. 18.83).



Fig. 18.83
Left fourth nerve palsy (*see text*)

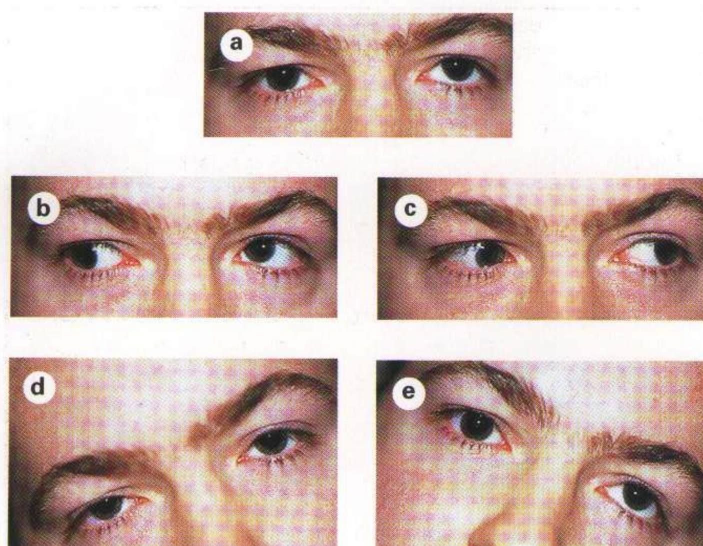


Fig. 18.84
Parks three step test. (**a**) Step 1; (**b** and **c**) step 2; (**d** and **e**) step 3 (*see text*)

- Excyclotorsion.
- Diplopia which is vertical, torsional and worse on looking down.
- Left hyperdeviation ('left over right') in the primary position when the uninvolved right eye is fixating due to weakness of the left superior oblique (Fig. 18.84a).
- The left hypertropia increases on right gaze (Fig. 18.84b) due to left inferior oblique overaction, and is minimal or absent in left gaze (Fig. 18.84c).

2. **Abnormal head posture** is adopted to avoid diplopia.
   - To intort the eye (alleviate excyclotorsion) there is contralateral head tilt.
   - To alleviate the inability to depress the eye in adduction, the face is turned to the right and the chin is depressed (*see* Fig. 16.16).

> ***NB:*** The left eye cannot look down and to the right, or intort; the head therefore does this and thus compensates.

3. **Bilateral** involvement is common and is characterized by:
   - Right hypertropia in left gaze, left hypertropia in right gaze.
   - Greater than 10° cyclodeviation on double Maddox rod test (*see* below).
   - V pattern esotropia.
   - Bilaterally positive Bielschowsky test (*see* below).

Special tests

1. **Parks three step test** is very useful in the diagnosis of fourth nerve palsy and is performed as follows:
   a. ***Step one***. Assess which eye is hypertropic in the primary position. Left hypertropia (*see* Fig. 18.84a) may be caused by weakness of one of the following four muscles: the depressors of the left eye (superior oblique or inferior rectus) or the elevators of the right eye (superior rectus or inferior oblique).
   b. ***Step two***. Determine whether the left hypertropia is greater in right gaze or left gaze (*see* Fig. 18.84b and c). Increase on left gaze implicates either the left inferior rectus or right inferior oblique. Increase on right gaze implicates either the left superior oblique or right superior rectus.
   c. ***Step three***. The Bielschowsky head tilt test isolates the paretic muscle. With the patient fixating a straight ahead target at 3 metres, the head is manually tilted to the right and then to the left. Increase of left hypertropia on left head tilt (*see* Fig. 18.84e) implicates the left superior oblique and increase of left hypertropia on right head tilt implicates the left inferior rectus.
2. **Double Maddox rod test**
   - Red and green Maddox rods, with the cylinders vertical, are placed one in front of either eye.
   - Each eye will therefore perceive a more or less horizontal line of light.
   - In the presence of cyclodeviation, the line perceived by the paretic eye will be tilted and therefore distinct from that of the other eye.
   - One Maddox rod is then rotated until fusion (superimposition) of the lines is achieved.
   - The amount of rotation can be measured in degrees and indicates the extent of cyclodeviation.
   - A unilateral fourth nerve palsy is characterized by less than 10° of cyclodeviation.

Causes of isolated fourth nerve palsy

1. **Congenital** lesions are frequent, although symptoms may not develop until adult life. Examination of old photographs for the presence of an abnormal head posture may be helpful as is the presence of an increased vertical prism fusional range.
2. **Trauma** frequently causes bilateral fourth nerve palsy. The long and slender nerves are vulnerable as they decussate in the anterior medullary velum through impact with the tentorial edge.
3. **Vascular** lesions are common but aneurysms and tumours are rare.

Sixth nerve

Applied anatomy

Nucleus

The nucleus of the sixth (abducens) nerve lies at the mid level of the pons, ventral to the floor of the fourth ventricle, where it is closely related to the horizontal gaze centre. The fasciculus of the seventh nerve curves around the abducent nucleus and produces an elevation in the floor of the fourth ventricle (facial

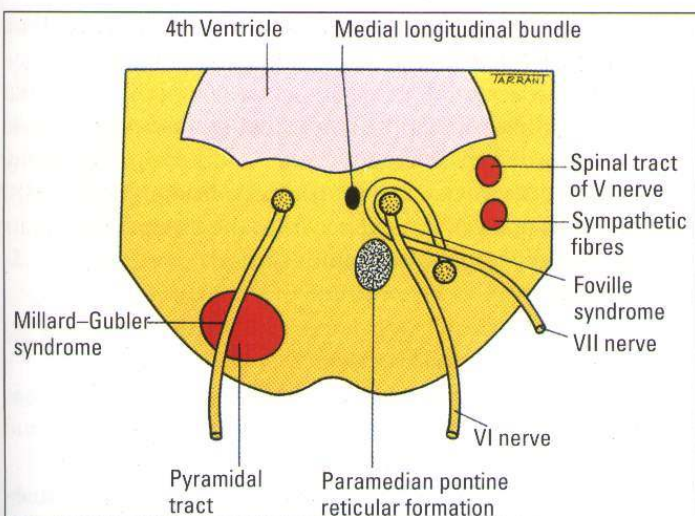


Fig. 18.85
The pons at the level of the sixth nerve nucleus

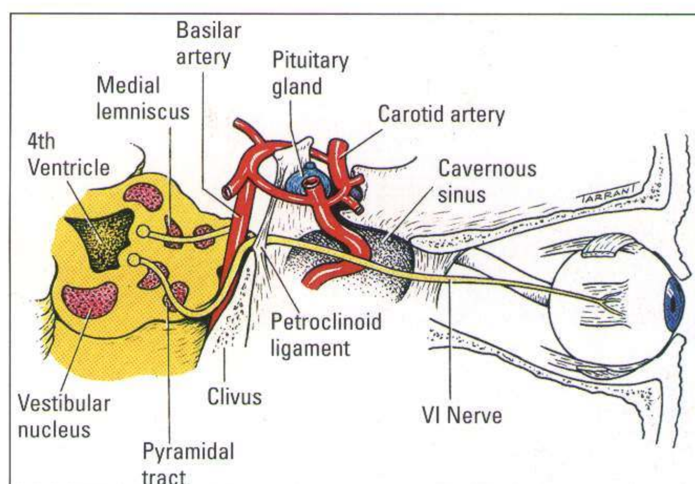


Fig. 18.86
Lateral view of the course of the sixth nerve

colliculus) (Fig. 18.85). An isolated sixth nerve palsy is therefore never nuclear in origin. A lesion in and around the sixth nerve nucleus causes the following signs:

- Ipsilateral weakness of abduction as a result of involvement of the sixth nerve.
- Failure of horizontal gaze towards the side of the lesion resulting from involvement of the horizontal gaze centre in the PPRF.
- Ipsilateral lower motor neurone facial nerve palsy caused by concomitant involvement of the facial fasciculus is also common.

Fasciculus

The fasciculus passes ventrally to leave the brain stem at the pontomedullary junction, just lateral to the pyramidal prominence.

1. **Foville syndrome** involves the fasciculus as it passes through the PPRF and is most frequently caused by vascular disease or tumours involving the dorsal pons. It is characterized by ipsilateral involvement of the fifth to eighth cranial nerves and central sympathetic fibres.
   - Fifth nerve: facial analgesia.
   - Sixth nerve palsy combined with a gaze palsy (PPRF).
   - Seventh nerve (nuclear or fascicular damage): facial weakness.
   - Eighth nerve: deafness.
   - Central Horner syndrome.
2. **Millard–Gubler** syndrome involves the fasciculus as it passes through the pyramidal tract and is most frequently caused by vascular disease, tumours or demyelination. It is characterized by the following:
   - Ipsilateral sixth nerve palsy.
   - Contralateral hemiplegia (since the pyramidal tracts decussate further inferiorly, in the medulla, to control contralateral voluntary movement).
   - Variable number of signs of a dorsal pontine lesion.

Basilar part

The basilar part leaves the brain stem at the pontomedullary junction and enters the prepontine basilar cistern. It then passes upwards close to the base of the skull and is crossed by the anterior inferior cerebellar artery (Fig. 18.86). It pierces the dura below the posterior clinoids and angles forwards over the tip of the petrous bone, passing through or around the inferior petrosal sinus, through Dorello canal (under the petroclinoid ligament), to enter the cavernous sinus. The following are important causes of damage to the basilar part of the nerve:

1. **Acoustic neuroma** may damage the sixth nerve at the pontomedullary junction (Fig. 18.87). It should be

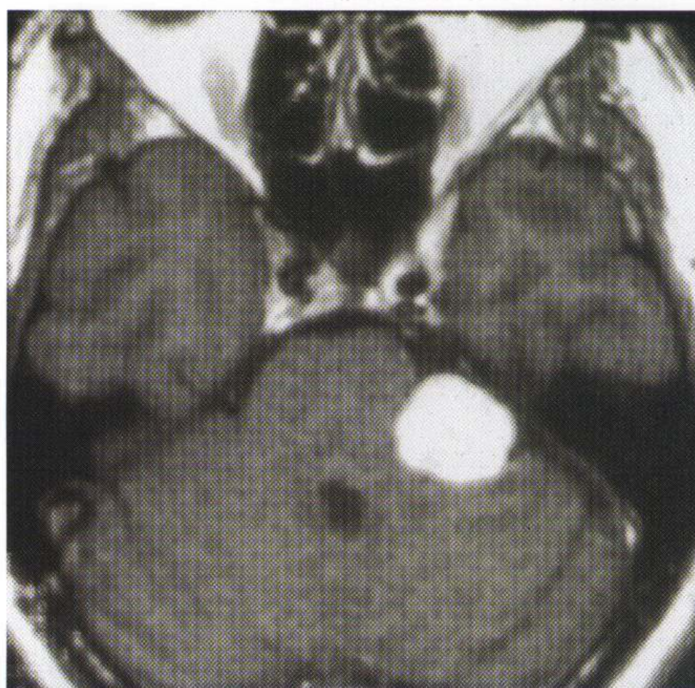


Fig. 18.87
Axial T1-weighted MRI scan with gadolinium showing an acoustic neuroma

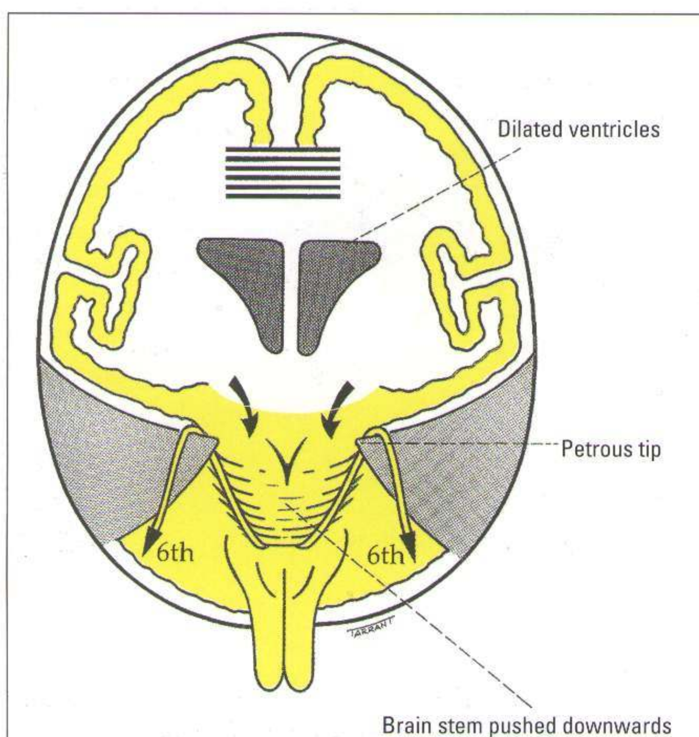


Fig. 18.88
Mechanism of bilateral sixth nerve palsies from raised intracranial pressure

emphasized that the first symptom of an acoustic neuroma is hearing loss and the first sign diminished corneal sensitivity. It is therefore very important to test hearing and corneal sensation in all patients with sixth nerve palsy.

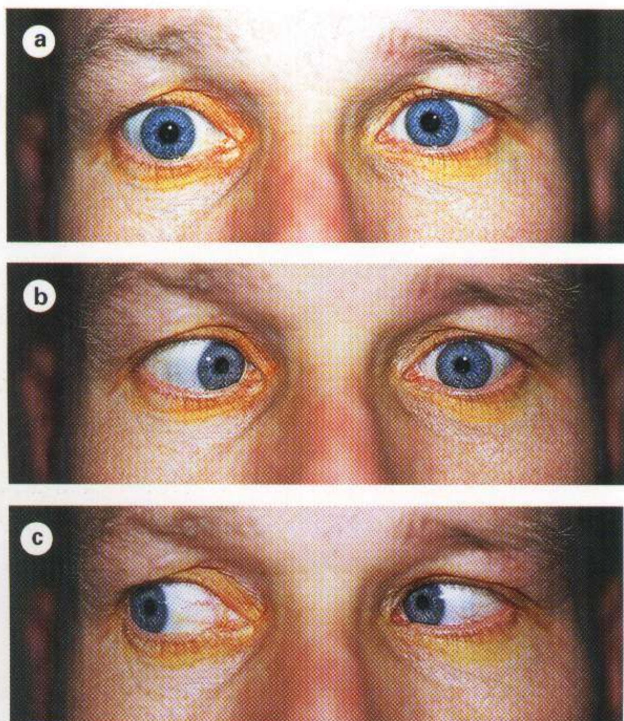


Fig. 18.89
Left sixth nerve palsy (*see text*)

2. **Nasopharyngeal tumours** may invade the skull and its foramina and damage the nerve during its basilar course.
3. **Raised intracranial pressure** caused by posterior fossa tumours or idiopathic intracranial hypertension may cause a downward displacement of the brain stem. This may stretch the sixth nerve over the petrous tip (Fig. 18.88) between its point of emergence from the brain stem and its point of entry into the cavernous sinus.

> *NB:* In this situation, sixth nerve palsy, which may be bilateral, is a false localizing sign.

4. **Basal skull fracture** may cause both unilateral and bilateral palsies.
5. **Gradenigo syndrome**, most frequently caused by mastoiditis or acute petrositis, may result in damage of the sixth nerve at the petrous tip. The latter is frequently accompanied by facial weakness and pain, and hearing difficulties.

Intracavernous and intraorbital parts

1. **The intracavernous part** runs forwards below the third and fourth nerves, as well as the first division of the fifth. Although the other nerves are protected within the wall of the sinus, the sixth is most medially situated and runs through the middle of the sinus in close relation to the internal carotid artery. It is therefore more prone to damage than the other nerves. Occasionally, an intracavernous sixth nerve palsy is accompanied by a postganglionic Horner syndrome (Parkinson sign) because in its intracavernous course the sixth nerve is joined by sympathetic branches from the paracarotid plexus. The causes of intracavernous sixth nerve and third nerve lesions are similar.
2. **The intraorbital part** enters the orbit through the superior orbital fissure within the annulus of Zinn to innervate the lateral rectus muscle.

Clinical aspects

Clinical features

1. **Signs** of a left sixth nerve palsy.
   - Left esotropia in the primary position due to unopposed action of the left medial rectus (Fig. 18.89a).
   - Marked limitation of left abduction due to weakness of the left lateral rectus (Fig. 18.89b).
   - Normal left adduction (Fig. 18.89c).
2. **Compensatory** face turn into the field of action of the paralysed muscle (i.e. to the left) to minimize diplopia, so that the eyes do not need to look towards the field of action of the paralysed muscle.
3. **Causes** of isolated sixth nerve palsies have already been mentioned.

> *NB:* Aneurysms rarely affect the sixth nerve but vascular causes are common.

Differential diagnosis

The following conditions may mimic sixth nerve palsy:

1. **Myasthenia gravis** can mimic virtually any ocular motility defect. Distinguishing features include variability of diplopia and other signs such as lid fatigue and Cogan twitch sign (*see* later).
2. **Restrictive thyroid myopathy** involving the medial rectus may give rise to limitation of abduction. Associated features include orbital and eyelid signs and a positive forced duction test (*see* Chapter 17).
3. **Medial orbital wall blowout fracture** with entrapment of the medial rectus giving rise to limitation of abduction (*see* Chapter 19).
4. **Orbital myositis** involving the lateral rectus is characterized by weakness of abduction and pain when this is attempted (*see* Chapter 17).
5. **Duane syndrome** is a congenital condition characterized by defective abduction and narrowing of the palpebral fissure on adduction (*see* Chapter 16).
6. **Convergence spasm** typically affects young adults and is characterized by convergence with miosis and increased accommodation.
7. **Divergence paralysis** is a rare condition which may be difficult to distinguish from unilateral or bilateral sixth nerve palsy. However, unlike sixth nerve palsy the esotropia may remain the same or diminish on lateral gaze.
8. **Infantile esotropia**

Chiasm

Applied anatomy

Pituitary gland

The sella turcica (Turkish saddle) is a deep saddle-shaped depression in the superior surface of the body of the sphenoid bone in which the pituitary gland lies (Fig. 18.90). The roof of the sella is formed by a fold of dura mater which stretches from the anterior to the posterior clinoids (diaphragma sellae). The optic nerves and chiasm lie above the diaphragma sellae; a visual field defect in a patient with a pituitary tumour therefore indicates suprasellar extension. Tumours less than 10 mm in diameter (microadenomas) often remain intrasellar, whereas those larger than 10 mm (macroadenomas) tend to manifest extrasellar extension. Posteriorly the chiasm is continuous with the optic tracts and forms the anterior wall of the third ventricle.

Chiasmal nerve pathways

Optic nerve fibres passing through the chiasm are arranged as follows:

1. **Lower nasal fibres** traverse the chiasm low and anteriorly. They are therefore most vulnerable to damage from expanding pituitary lesions, so the upper temporal quadrants of the visual fields are involved first.

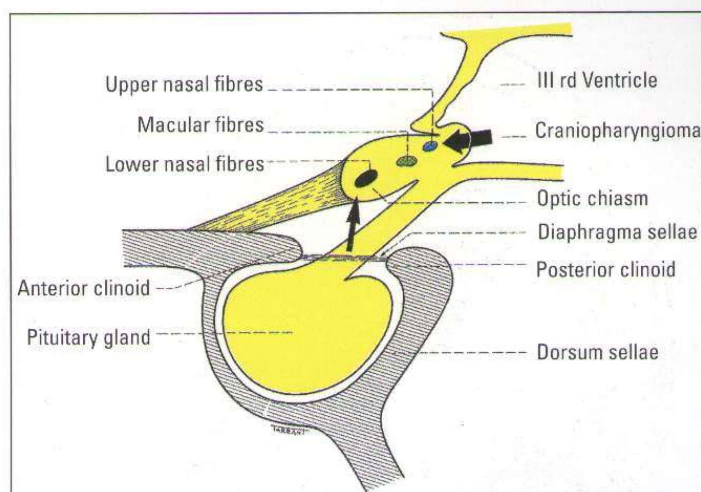


Fig. 18.90
Anatomy of the optic chiasm in relation to the pituitary gland

> ***NB:*** The inferonasal fibres loop forwards into the contralateral optic nerve, before passing posteriorly into the optic tract (anterior knee of Wilbrand) and may therefore be affected by lesions affecting the posterior part of the optic nerve.

2. **Upper nasal fibres** traverse the chiasm high and posteriorly and therefore are involved first by lesions coming from above the chiasm (e.g. craniopharyngiomas). If the lower temporal quadrants of the visual field are affected more than the upper, a pituitary adenoma is unlikely.
3. **Macular fibres** decussate throughout the chiasm.

Anatomical variants

The following anatomical variations in the location of the chiasm may have important clinical significance (Fig. 18.91):

1. **Central chiasm**, which is present in about 80% of normals, lies directly above the sella so that expanding pituitary tumours will involve the chiasm first.
2. **Prefixed chiasm**, which is present in about 10% of normals, is located more anteriorly, over the tuberculum sellae, so that pituitary tumours involve the optic tracts first.
3. **Postfixed chiasm**, which is present in the remaining 10% of normals, is located more posteriorly, over the dorsum sellae, so that pituitary tumours are apt to damage the optic nerves first.

Parachiasmal vascular structures

1. **The cavernous sinuses** lie lateral to the sella so that laterally expanding pituitary tumours affect the cavernous sinus and may damage the intracavernous parts of the

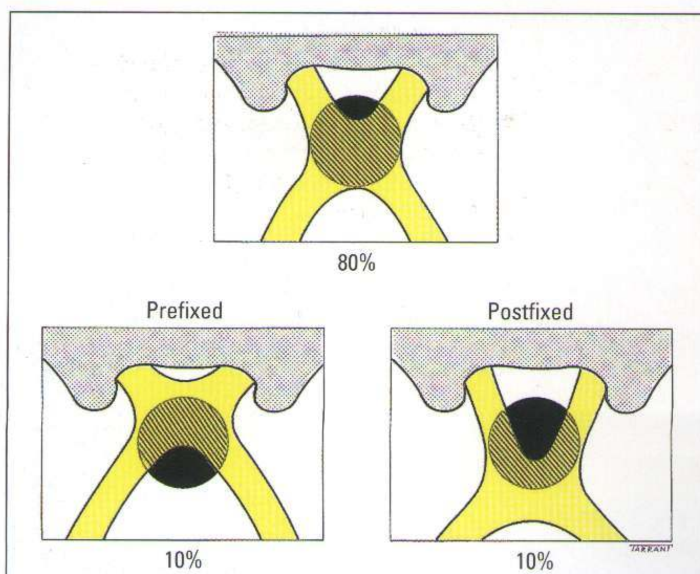


Fig. 18.91
Anatomical variations in position of the optic chiasm

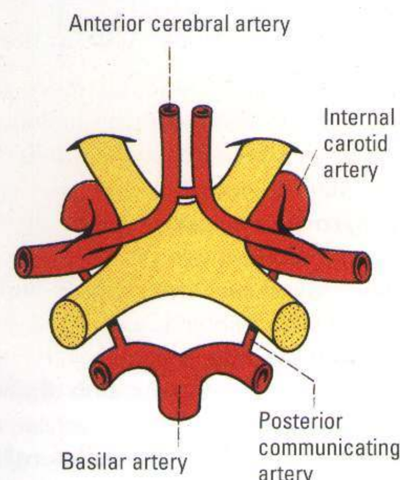


Fig. 18.92
Relationship between the chiasm and adjacent arteries

third, fourth and sixth cranial nerves. Conversely, aneurysms arising from the intracavernous part of the internal carotid artery may erode into the sella and mimic pituitary tumours.

2. **The internal carotid arteries** curve posteriorly and upwards from the cavernous sinus and lie immediately below the optic nerves (Fig. 18.92). They then ascend vertically alongside the lateral aspect of the chiasm. The precommunicating portion of the anterior cerebral artery is closely related to the superior surface of the chiasm and optic nerves. An aneurysm in this region can therefore compress the optic nerve (Fig. 18.93) or the chiasm.

Applied physiology

Pituitary hormones

The lobules of the anterior part of the pituitary gland are composed of six cell types. Five of these secrete hormones and the sixth (follicular cell) has no secretory function. The hormones secreted by the anterior pituitary gland are growth hormone (GH), prolactin, follicle-stimulating hormone (FSH), adrenocorticotrophic hormone (ACTH), thyroid-stimulating hormone (TSH), leutenizing hormone (LH) and beta-lipotrophin. Although pituitary adenomas are classified as basophil, acidophil and chromophobe, tumours of mixed-cell types are common and any of the six cell types may proliferate to produce an adenoma. The anterior pituitary is itself under the control of the various inhibiting and releasing factors which are synthesized in the hypothalamus and which pass to the anterior pituitary through the hypothalamo-hypophyseal portal system.

Causes of pituitary dysfunction

1. **Hyperpituitarism** (Fig. 18.94)
   a. ***Basophil tumours*** secrete ACTH and cause Cushing disease (*see* Chapter 20).
   b. ***Acidophil tumours*** secrete growth hormone, which causes gigantism in children and acromegaly in adults (*see* Chapter 20).
   c. ***Chromophobe adenomas*** may secrete prolactin and are referred to as prolactinomas. Excessive levels of prolactin in women lead to the infertility–amenorrhoea–galactorrhoea syndrome, and in men cause hypogonadism, impotence, sterility, decreased libido and occasionally gynaecomastia and even galactorrhoea. Some chromophobe adenomas are non-secreting.
2. **Hypopituitarism**
   a. ***Direct pressure*** on the secreting cells in the anterior pituitary by a mass. Secondary deposits are common in the pituitary but do not normally affect hormone secretion.
   b. ***Vascular damage*** to the pituitary (e.g. pituitary apoplexy after childbirth—Sheehan syndrome).
   c. ***Iatrogenic*** causes such as pituitary surgery and/or radiotherapy.
   d. ***Interference*** with the synthesis of inhibiting and releasing factors in the hypothalamus by gliomas or impediment of their transport in the portal system.

NB: The clinical features are dictated by both the pattern of hormone deficiency and the stage of growth and development of the patient at the time. Usually gonadotrophin secretion is impaired first, followed by that of growth hormone; deficiencies in other hormones occur later.

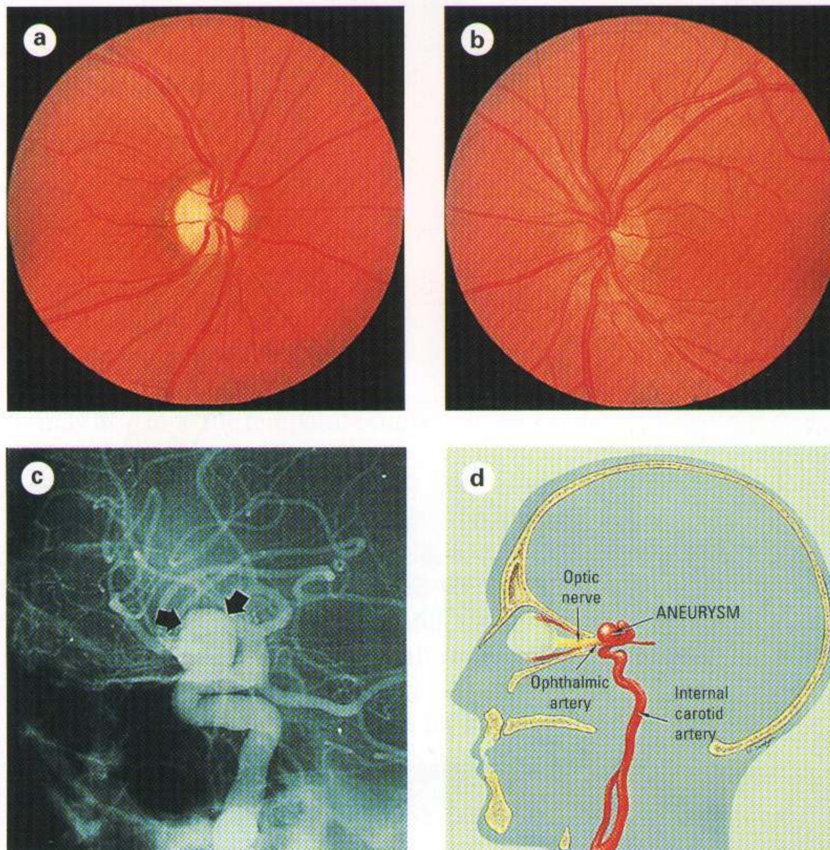


Fig. 18.93
Aneurysmal compression of the right optic nerve. (**a**) Right optic atrophy; (**b**) normal left disc; (**c**) angiogram showing the aneurysm (arrows); (**d**) schematic diagram (Courtesy of Wilmer Institute)

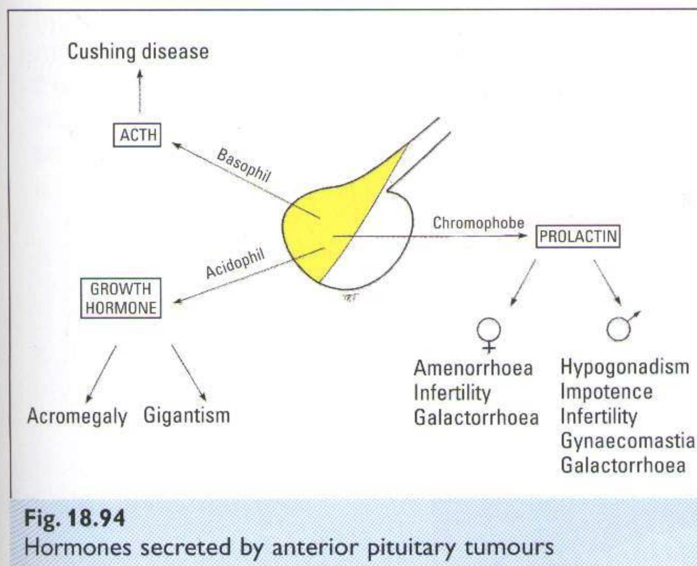


Fig. 18.94
Hormones secreted by anterior pituitary tumours

Causes of chiasmal disease

1. **Tumours** such as pituitary adenomas, craniopharyngiomas, meningiomas, gliomas, chordomas, dysgerminomas, nasopharyngeal tumours and metastases.
2. **Non-neoplastic masses** such as aneurysms, Rathke pouch cysts, fibrous dysplasia, sphenoidal sinus mucoceles and arachnoid cysts.
3. **Miscellaneous disorders** including demyelination, inflammation, trauma, radiation-induced necrosis and vasculitis.

Pituitary adenoma

Clinical features

The chromophobe adenoma is the most common primary intracranial tumour to produce neuro-ophthalmological features. Although generally detected by endocrinologists, non-secreting tumours may first present to ophthalmologists.

1. **Presentation** is typically during early adult life or middle age and only occasionally in the elderly with the following:
   a. *Headache* may be prominent due to involvement of pain-sensitive fibres in the diaphragma sellae. As the tumour expands upwards and breaks through the diaphragma the headaches may stop. The headache is non-specific and does not have the usual features associated with raised intracranial pressure. Diagnostic delay is therefore common in the absence of obvious endocrine disturbances.
   b. *Visual symptoms* usually have a very gradual onset and may not be noticed by the patient until well established. It is therefore essential to examine the visual function in all patients with non-specific headaches or endocrine disturbances.
2. **Visual field defects** depend on the anatomical relationship between the pituitary and chiasm.
   - If the chiasm is central, both superotemporal fields are affected first, as the tumour grows upwards and splays

the anterior chiasmal notch, compressing the crossing inferonasal fibres (Fig. 18.95).

- The defects then progress into the lower temporal fields. As tumour growth is often asymmetrical, the degree of visual field loss is usually different on the two sides.
- Patients may not present until central vision is affected from pressure on the macular fibres. The eye with the greater field loss usually also has more marked impairment of visual acuity.

> ***NB:*** The absence of a visual field defect does not exclude a pituitary tumour, since tumours confined to the sella are often visually asymptomatic. Acidophil adenomas do not expand beyond the sella as frequently as chromophobe adenomas, and basophil adenomas are usually small and rarely compress the chiasm.

3. **Differential diagnosis** of bitemporal defects includes dermatochalasis of the upper eyelids, tilted discs (Fig. 18.96), optic nerve colobomas, nasal retinoschisis, nasal retinitis pigmentosa and functional visual loss.

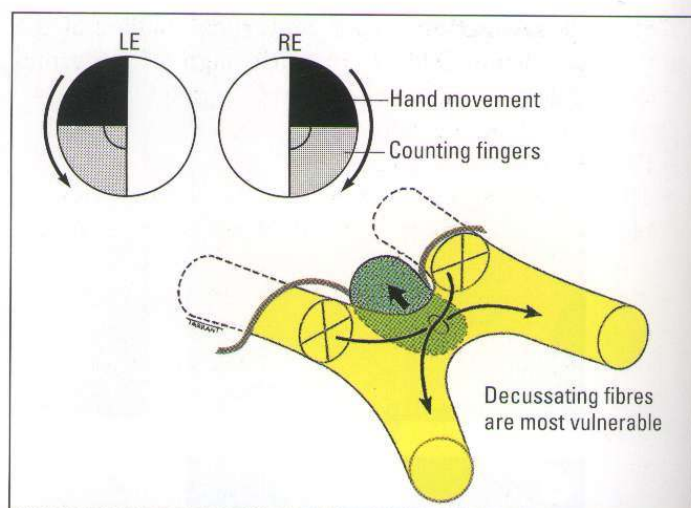


Fig. 18.95
Progression of bitemporal visual field defects caused by compression of the chiasm from below by a pituitary adenoma

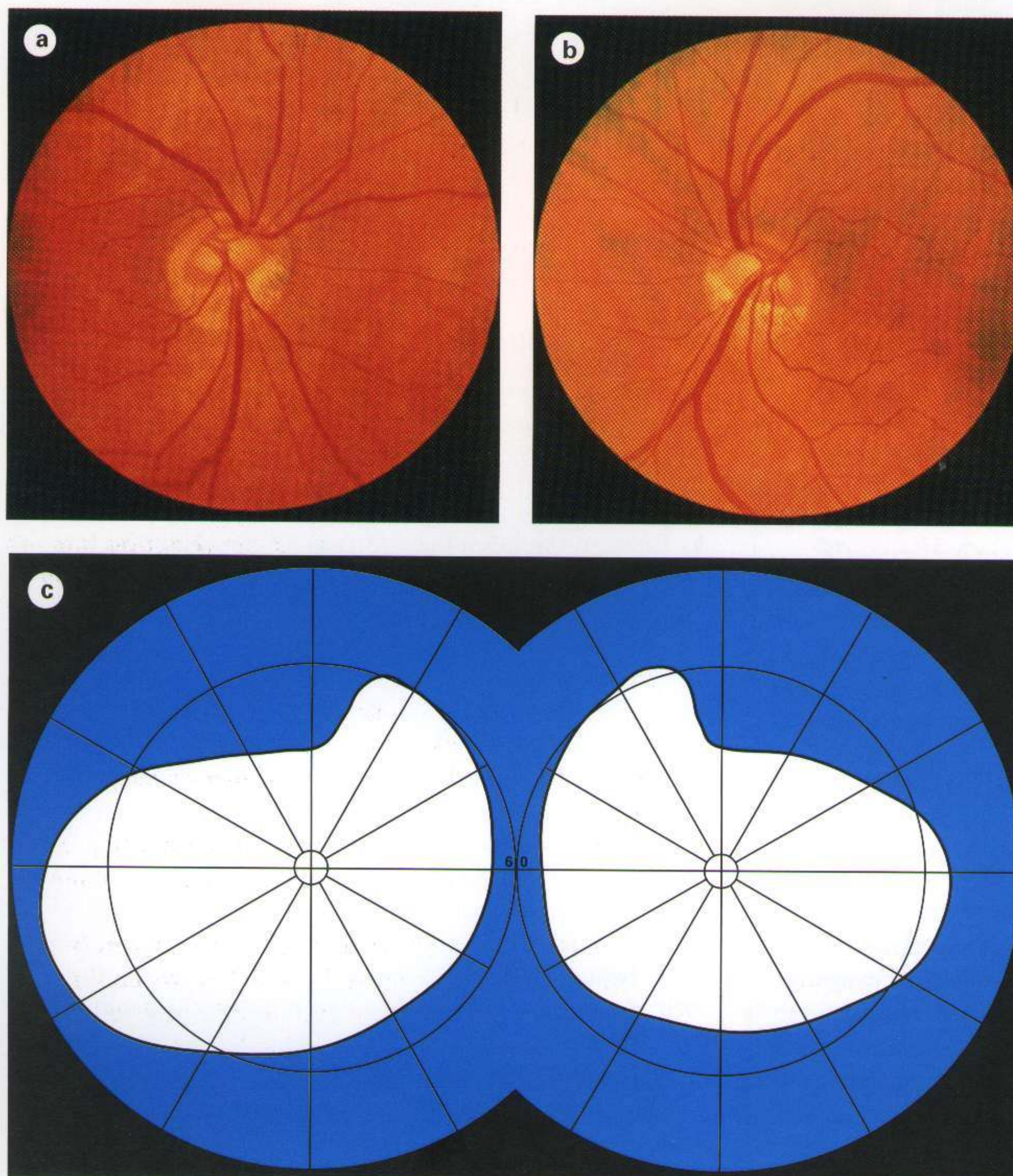


Fig. 18.96
(**a** and **b**) Tilted discs; (**c**) associated bitemporal visual field defects which do not respect the vertical midline
(Courtesy of Wilmer Institute)

4. **Colour desaturation** across the vertical midline of the uniocular visual field is an early sign of chiasmal compression which can be detected very simply with a red pin or a red Mydriacyl bottle top.
   - Each eye is tested separately.
   - The patient is asked to compare the colour and intensity of the target as it is brought from the nasal to the temporal visual field.
   - Another technique is to simultaneously present red targets in precisely symmetrical parts of the temporal and nasal visual fields, and to ask if the colours appear the same.
   - Patients may also miss the temporal number on Ishihara testing.
5. **Optic atrophy** is present in approximately 50% of cases with field defects caused by pituitary lesions. Patients are invariably more aware of difficulties with central vision (e.g. when reading) than with peripheral vision. It is therefore important to perform very careful visual field examinations on both eyes in patients with unexplained unilateral deterioration of central vision. When optic atrophy is present the prognosis for visual recovery after treatment is guarded. When nerve fibre loss is confined to fibres originating in the nasal retina (i.e. nasal to the fovea), only the nasal and temporal aspects of the disc will be involved, resulting in a band or 'bow-tie'-shaped atrophy.
6. **Miscellaneous features** include diplopia as a result of lateral expansion into the cavernous sinus and involvement of ocular motor nerves and, rarely, see-saw nystagmus of Maddox.
7. **Pituitary apoplexy** is a rare condition caused by a sudden increase in the size of a pituitary tumour, often secondary to haemorrhage.
   a. Presentation is with severe headache, diplopia, visual loss and photophobia.
   b. Signs include ophthalmoplegia, decreased sensation over the distribution of the first and second divisions of the trigeminal nerve and variable visual loss.
   c. Treatment with systemic steroids and surgery may be necessary to prevent blindness and other neurological complications.

Special investigations

1. **MRI** demonstrates the relationship between a mass lesion and the chiasm. The optimal study consists of coronal, axial and sagittal thin sections through the chiasm and optic nerves before and after gadolinium injection. The coronal plane is optimal for demonstrating sellar contents. Pituitary adenomas are typically hypointense on T1 images, hyperintense on T2 images and enhance strongly with gadolinium in a heterogeneous fashion (Fig. 18.97 and *see* Fig. 18.7). Repeated MRI to monitor progress is safe because there is no ionizing radiation risk.
2. **CT** will demonstrate enlargement or erosion of the sella.

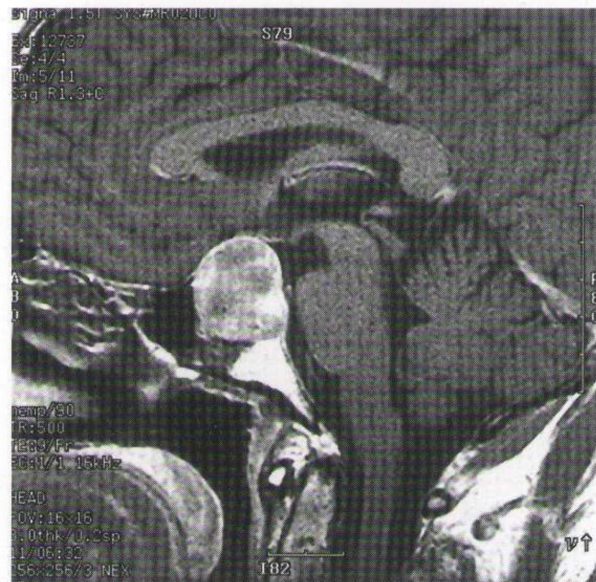


Fig. 18.97
Sagittal T1-weighted gadolinium-enhanced MRI scan showing a pituitary adenoma (Courtesy of D. Thomas)

3. **Endocrinological** evaluation should be tailored to the individual patient. All patients suspected of having a pituitary adenoma should have assays of serum prolactin, FSH, TSH and growth hormone. An insulin stress test may also be required in selected cases. Patients with large adenomas with visual field defects are at some risk of pituitary apoplexy if the hypoglycaemic response is profound.

Treatment

Not all tumours require treatment; observation may be appropriate for incidentally discovered and clinically silent tumours.

1. **Medical** therapy to shrink a prolactin-secreting tumour involves dopamine agonists such as cabergoline or bromocriptine. Patients with significant visual field defects should have urgent prolactin level assay and, if elevated, treatment should be started as soon as possible. Visual function may improve within hours. Endocrine function also often improves with cessation of galactorrhoea, improvement of libido and return of menstruation.
2. **Surgery**
   a. Indications are mass effects causing severe compressive problems or failure to respond to medical therapy or radiotherapy.
   b. Technique. Hypophysectomy is most frequently performed through a trans-sphenoidal approach through the upper gum under the lips. Occasionally both trans-sphenoidal hypophysectomy and a craniotomy are required to remove tissue above the diaphragma sellae.
   c. Visual recovery is triphasic.

- An early fast phase in the first week may lead to normalization of visual fields in some patients.
- A subsequent slow phase between 1 and 4 months is the period of most notable improvement.
- A late phase (6 months to 3 years) of mild improvement follows.

3. **Radiotherapy** is often used as an adjunct following incomplete removal of tumour. It can also be used as primary treatment in selected cases. While usually effective in preventing further tumour growth it is often less successful in controlling abnormal hormone secretion.
4. **Gamma knife** stereotactic radiotherapy is a relatively new method of delivering a concentrated dose of radiation to the tumour with little radiation to surrounding tissues. It is therefore of particular value in treating adenomas in close proximity to the optic nerve or when the cavernous sinus is invaded.

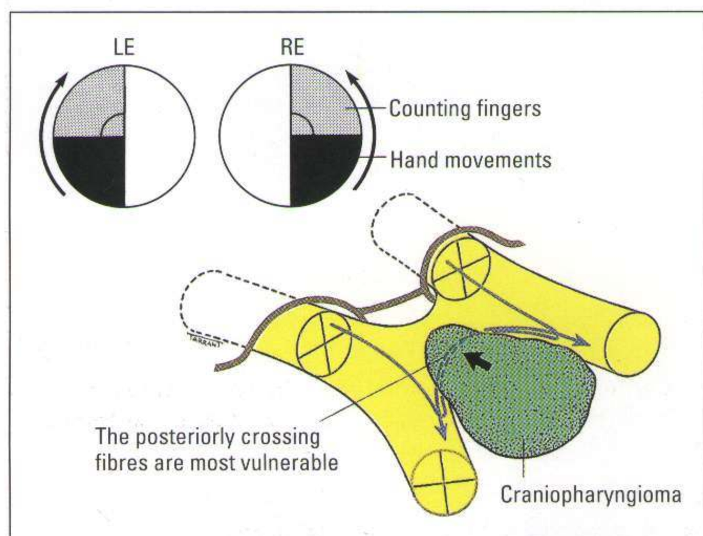


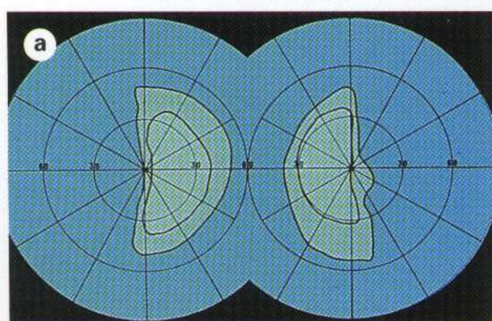
Fig. 18.98
Progression of bitemporal visual field defects caused by compression of the chiasm from above by a craniopharyngioma



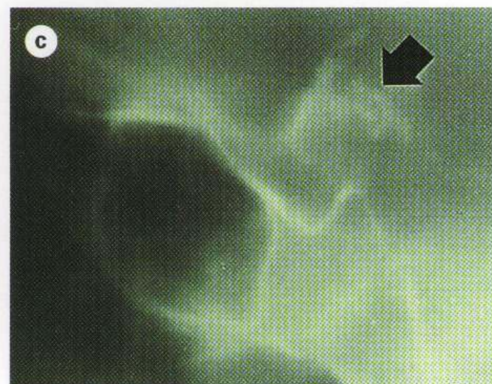
Fig. 18.99
Sagittal T1-weighted MRI scan showing a craniopharyngioma
(Courtesy of K. Nischal)

Craniopharyngioma

The craniopharyngioma is a slow-growing tumour arising from vestigial remnants of Rathke pouch along the pituitary stalk.







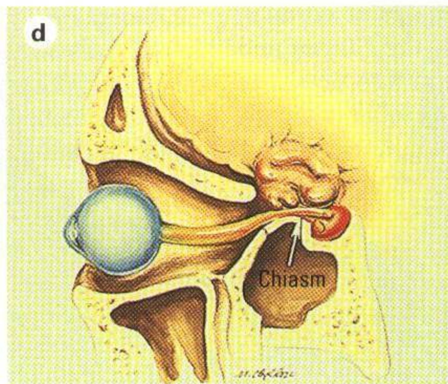


Fig. 18.100
Craniopharyngioma. (**a**) Bitemporal hemianopia; (**b**) axial CT scans showing calcification; (**c**) plain radiograph showing calcification; (**d**) chiasmal compression from above
(Courtesy of Wilmer Institute)

1. **Presentation** depends on the age of the patient:
   a. *Children* frequently present with dwarfism, delayed sexual development and obesity due to interference with hypothalamic function.
   b. *Adults* usually present with visual impairment and visual field defects.
2. **Visual field defects** are complex and may be due to involvement of the optic nerves, chiasm or tracts.
   - The initial defect frequently involves both inferotemporal fields because the tumour compresses the chiasm from above and behind, damaging the upper nasal fibres (Fig. 18.98).
   - The defects then spread to involve the upper temporal fields.
3. **MRI** shows the location of the tumour but not calcification which is present in 50–70% of cases. A solid tumour appears isointense on T1 images (Fig. 18.99). Cystic components appear hyperintense on T1 images.
4. **CT** (Fig. 18.100b) and plain films (Fig. 18.100c) demonstrate calcification but this is not diagnostic of craniopharyngioma because it may also be found in other parachiasmal lesions such as meningiomas, aneurysms and chordomas.
5. **Treatment** is mainly surgical, although intimacy to the chiasm may preclude complete removal. Postoperative radiotherapy may be helpful, but recurrences are common, necessitating lifelong follow-up.

Meningioma

Intracranial meningiomas typically affect middle-aged women. Visual field defects and clinical signs depend on the location of the tumour.

1. **Tuberculum sellae** meningiomas typically compress the junction of the chiasm with the optic nerve. This gives rise to an ipsilateral central scotoma caused by optic nerve

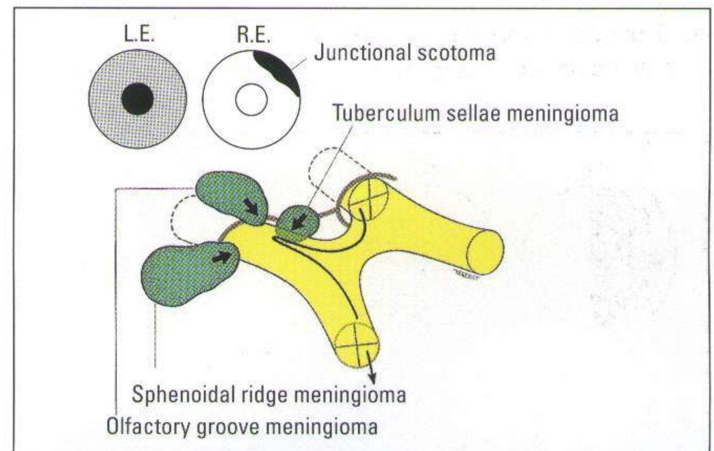


Fig. 18.101
Intracranial optic nerve compression by meningiomas and visual field defect caused by a tuberculum sellae meningioma

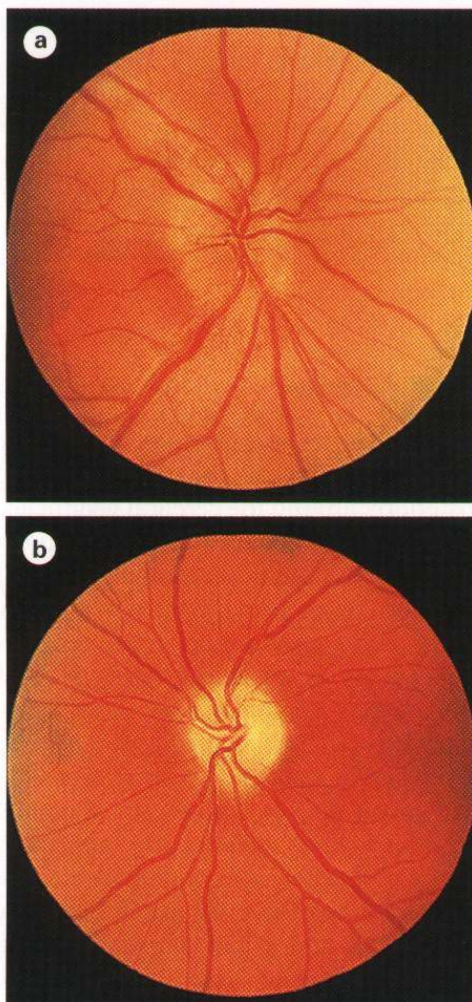
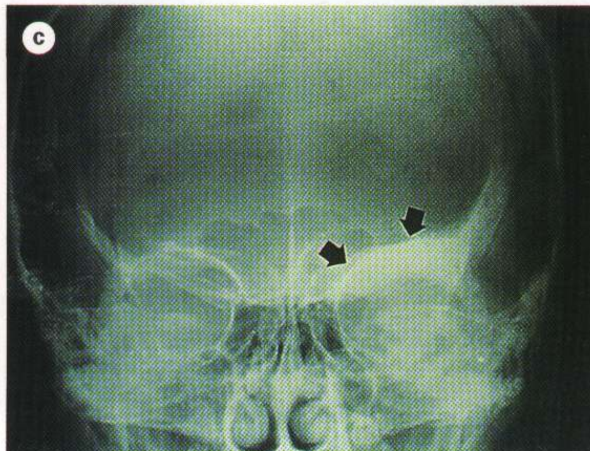


Fig. 18.102
Optic nerve compression by left sphenoidal ridge meningioma. (**a**) Disc swelling; (**b**) optic atrophy; (**c**) plain radiograph showing hyperostosis (arrows)
(Courtesy of Wilmer Institute)



compression and a contralateral upper temporal defect (junctional scotoma) due to damage to the anterior knee of Wilbrand (Fig. 18.101).

2. **Sphenoidal ridge** meningiomas compress the optic nerve early if the tumour is located medially and late if the lateral aspect of the sphenoid bone and middle cranial fossa are involved (Figs 18.102 and 18.103). A classic finding in the latter is fullness in the temporal fossa as a result of hyperostosis (Fig. 18.104).



Fig. 18.103
Axial T2-weighted MRI scan showing a left sphenoidal ridge meningioma (Courtesy of D. Thomas)



Fig. 18.104
Right sphenoidal ridge meningioma causing reactive hyperostosis and proptosis

3. **Olfactory groove** meningioma may cause loss of the sense of smell, as well as optic nerve compression.
4. **Treatment** is surgical but postoperative radiotherapy is frequently used in the event of incomplete excision.

Optic tract

Introduction

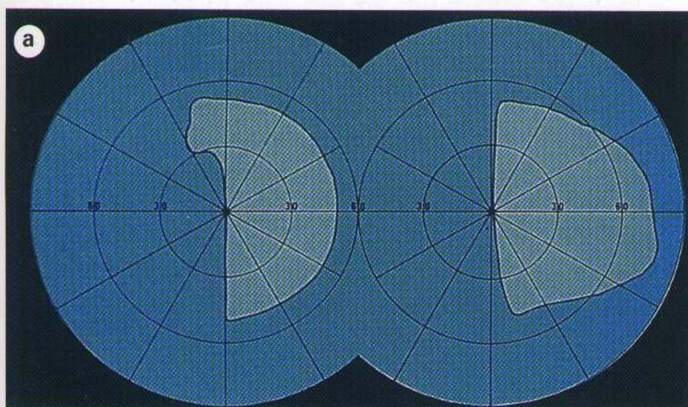
Retrochiasmal pathology results in binocular visual field defects involving contralateral visual space. Both eyes therefore manifest partial or total visual hemifield loss opposite the side of a retrochiasmal lesion. Such a 'hemianopia' involving the same side of visual space in both eyes is homonymous, in contradistinction to that seen in chiasmal compression, which produces heteronymous (bitemporal) hemianopia, in which opposite sides of the visual field are affected in each eye.

Incongruity

A homonymous hemianopia may be incomplete or complete. In the context of incomplete hemianopia, congruity refers to how closely the extent and pattern of field loss in one eye matches that of the other. Almost identical field defects in either eye are therefore highly congruous, while mismatching right and left visual field defects are incongruous. Hemianopia secondary to pathology in the anterior retrochiasmal visual pathways is characteristically incongruous, while that due to pathology further back (i.e. the posterior optic radiations) manifests a high degree of congruity.

Clinical features

1. **Homonymous hemianopia**. The optic tracts arise at the posterior aspect of the chiasm, diverge and extend posteriorly around the cerebral peduncles, to terminate in the lateral geniculate bodies. Each optic tract contains crossed fibres from the contralateral nasal hemiretina, and uncrossed fibres from the ipsilateral temporal hemiretina. Nerve fibres originating from corresponding retinal elements are, however, not closely aligned. Homonymous hemianopias caused by optic tract lesions are therefore characteristically incongruous (Fig. 18.105a). Lesions of the lateral geniculate body also produce asymmetrical hemianopic defects. The causes of optic tract disease are similar to those affecting the chiasm but the tract is particularly vulnerable when the chiasm is pre-fixed.
2. **Wernicke hemianopic pupil**. The optic tracts contain both visual and pupillomotor fibres. The visual fibres terminate in the lateral geniculate body but the pupillary



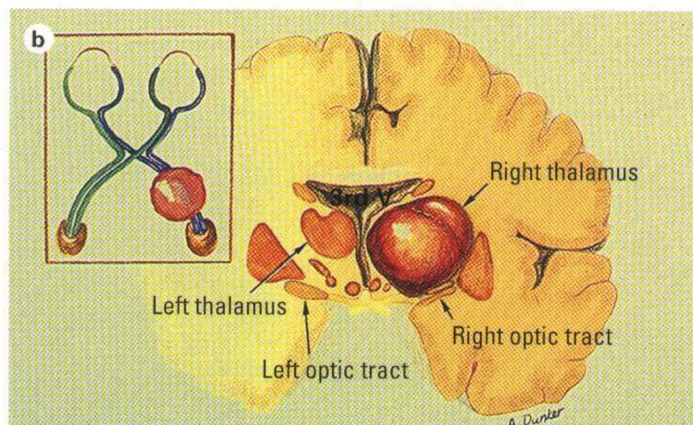


Fig. 18.105
Optic tract lesion. (**a**) Incongruous homonymous hemianopia; (**b**) location of lesion (Courtesy of Wilmer Institute)

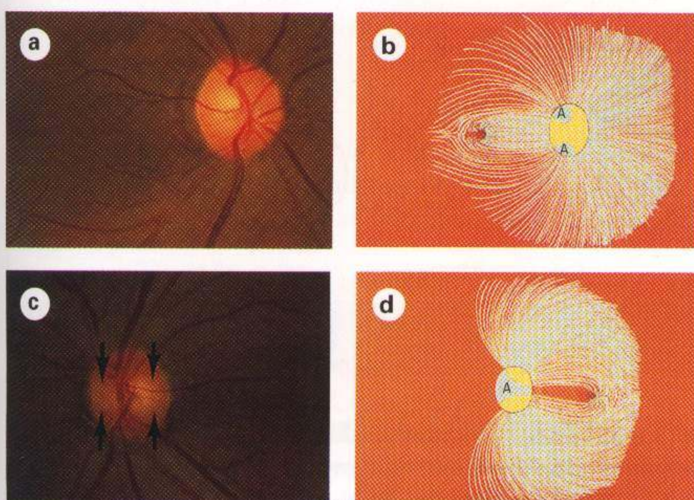


Fig. 18.106
Optic atrophy due to a right optic tract lesion. (**a** and **b**) Ipsilateral eye; (**c** and **d**) contralateral eye (*see text*) (Courtesy of Wilmer Institute)

fibres leave the optic tract anterior to the lateral geniculate body, projecting through the brachium of the superior colliculus to terminate in the pretectal nuclei. An optic tract lesion may therefore give rise to an afferent pupillary conduction defect. Characteristically, the pupillary light reflex will be normal when the unaffected hemiretina is stimulated, and absent when the involved hemiretina is stimulated (i.e. light is shone from the hemianopic side). In practice, this Wernicke hemianopic pupillary reaction is difficult to elicit because of scatter of light within the eye; hence the need for a very fine beam of light.

3. **Optic atrophy** may result when the optic tracts are damaged because the fibres in the optic tract are the axons of the retinal ganglion cells. The ipsilateral disc manifests atrophy of the superior and inferior aspects of the neuroretinal rim (fibres from the temporal retina) (Fig. 18.106a and b), while the contralateral disc manifests a bow-tie pattern of atrophy (nasal retinal fibres) (Fig. 18.106c and d).
4. **Contralateral pyramidal signs** may occur when an optic tract lesion also damages the ipsilateral cerebral peduncle.

Optic radiations

Applied anatomy

The optic radiations extend from the lateral geniculate body to the striate cortex, which is located on the medial aspect of the occipital lobe, above and below the calcarine fissure (Fig. 18.107). The optic radiations and visual cortex have a dual blood supply from the middle and posterior cerebral arteries. As the radiations pass posteriorly, fibres from corresponding retinal elements lie progressively closer together. For this reason, incomplete hemianopias caused by lesions of the posterior radiations are more congruous than those involving the anterior radiations. Because these fibres are third-order neurones that originate in the lateral geniculate body, lesions of the optic radiations do not produce optic atrophy.

Temporal radiations

1. **Visual field defect** consists of a contralateral, homonymous, superior quadrantanopia ('pie in the sky'), because the inferior fibres of the optic radiations, which subserve the upper visual fields, first sweep antero-inferiorly into the temporal lobe (Meyer loop) around the anterior tip of the temporal horn of the lateral ventricle (Fig. 18.107a).
2. **Associated features** include contralateral hemisensory disturbance and mild hemiparesis, because the temporal radiations pass very close to the sensory and motor fibres of the internal capsule before passing posteriorly and rejoining the superior fibres. Other features of temporal lobe disease include paroxysmal olfactory and gustatory hallucinations (uncinate fits), formed visual hallucina-

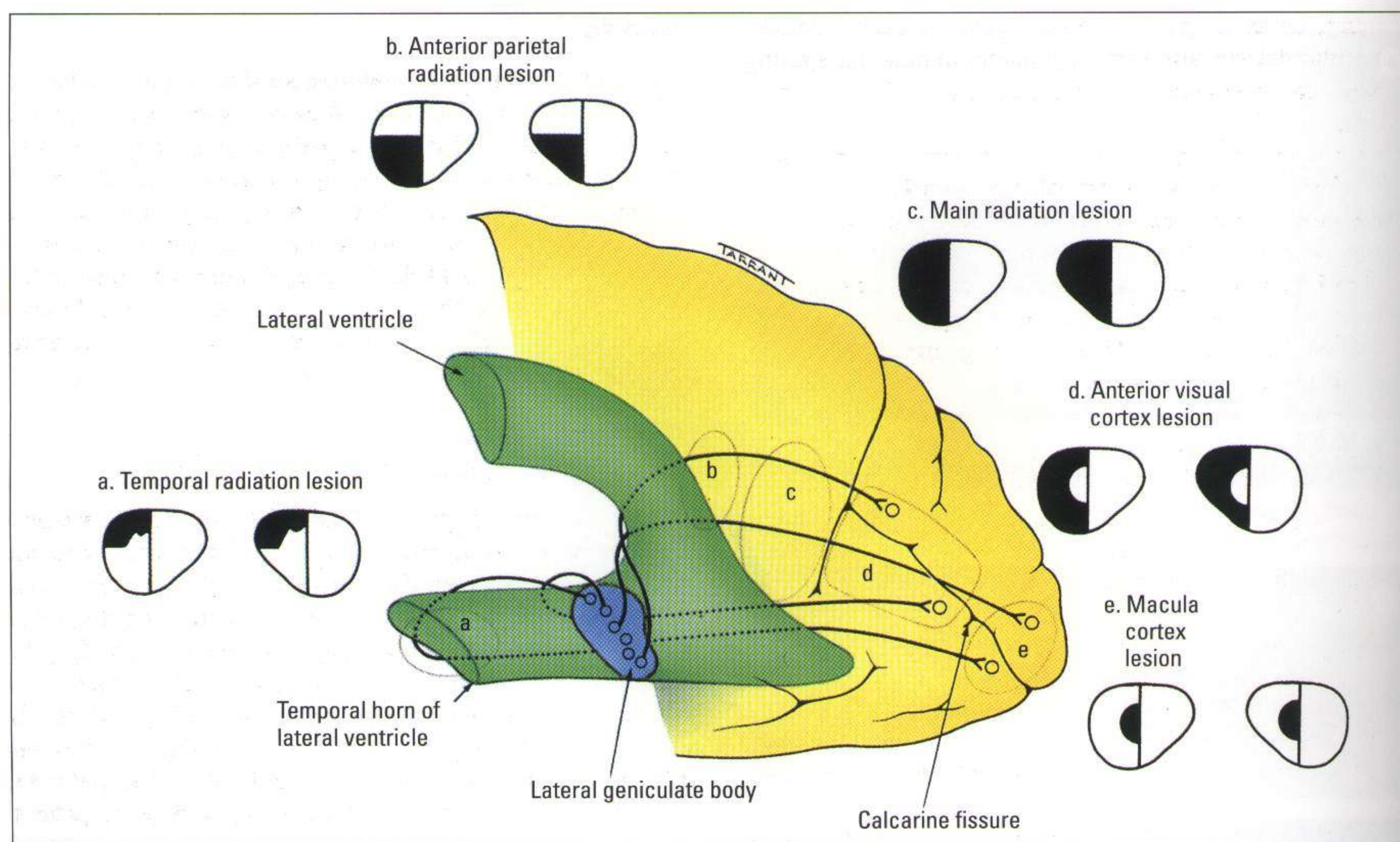


Fig. 18.107
Visual field defects caused by lesions of the optic radiations and visual cortex

tions, seizures and receptive dysphasia if the dominant hemisphere is involved.

Anterior parietal radiations

1. **Visual field defect** consists of a contralateral, homonymous, inferior quadrantanopia ('pie on the floor') because the superior fibres of the radiations, which subserve the inferior visual fields, proceed directly posteriorly through the parietal lobe to the occipital cortex. A lesion involving only the anterior parietal part of the radiations is, however, very rare. In general, hemianopias resulting from parietal lobe lesions tend to be relatively congruous (Fig. 18.107b).
2. **Associated features** of parietal lobe disease include agnosias, visual perception difficulties (particularly with right parietal lesions), right–left confusion and acalculia (particularly with left parietal lesions).

Main radiations

Deep in the parietal lobe, the optic radiations lie just external to the trigone and the occipital horn of the lateral ventricle. Lesions in this area usually cause a complete homonymous hemianopia (Fig. 18.107c). Optokinetic nystagmus (OKN) may be useful in localizing a lesion causing an isolated homonymous hemianopia that does not conform to any set pattern in a patient without associated neurological deficits. Normally OKN involves smooth pursuit of a target, followed by a saccade in the opposite direction to fixate on the next target. If the optomotor pathways in the posterior hemisphere are damaged, the OKN response will be diminished when targets are rotated towards the side of the lesion (i.e. away from the hemianopia). This is explained on the basis that the occipital lobe can no longer control ipsilateral pursuit, while the contralateral hemianopia inhibits refixational saccades. This is called the positive OKN sign. The combination of a homonymous hemianopia and OKN asymmetry therefore suggests a lesion involving the posterior optic radiations. Rarely occipital lobe lesions may also cause OKN asymmetry.

Striate cortex

Clinical features

1. **Visual field defects**. In the striate cortex the peripheral visual fields are represented anteriorly. This part of the occipital lobe is supplied by a branch of the posterior cerebral artery. Central macular vision is represented posteriorly just lateral to the tip of the calcarine cortex, an area supplied mainly by a branch of the middle cerebral artery. Occlusion of the posterior cerebral artery will therefore tend to produce a macular-sparing congruous homonymous hemianopia (Fig. 18.107d). Damage to the tip of the occipital cortex, as might occur from a head

injury, tends to give rise to congruous, homonymous, macular defects, although asymmetrical macular sparing may sometimes occur with vascular lesions of the occipital lobe.

> *NB:* The anterior-most part of the calcarine cortex subserves the temporal extremity of the visual field of the contralateral eye, the area of visual space that extends beyond the field of binocular single vision and is perceived monocularly. A lesion in this area may therefore give rise to a monocular temporal field defect in the contralateral eye, known as a temporal crescent.

2. **Associated features** of visual cortex disease (cortical blindness) are: (a) formed visual hallucinations, particularly involving the hemianopic field, (b) denial of blindness (Anton syndrome) and (c) Riddoch phenomenon, characterized by the ability to perceive kinetic, but not static targets.

Causes

1. **Vascular lesions** in the territory of the posterior cerebral artery are responsible for over 90% of isolated homonymous hemianopias with no other neurological deficits.
2. **Other causes**, which are less common, include migraine, trauma and primary or metastatic tumours.

Higher visual function

From the striate cortex (area 17), visual information is relayed to the visual association areas (18 and 19) of the cerebral cortex, where it is processed, analysed and interpreted. Lesions of various areas of the cerebral cortex produce characteristic clinical pictures.

Alexia and agraphia

The angulate gyrus of the dominant hemisphere (commonly the left) subserves the ability to write. Visual information from both occipital cortices is relayed to the left angulate gyrus, fibres from the right side crossing the midline in the splenium of the corpus callosum. Alexia (the inability to read), commonly accompanied by agraphia (the inability to write), may be produced by lesions of the angulate gyrus of the dominant cerebral hemisphere. Alexia may occur independently of agraphia in the context of a left occipital lesion of sufficient magnitude to involve fibres crossing the splenium, from the right occipital cortex to the left angulate gyrus. The clinical features consist of a right homonymous hemianopia with alexia, since information from the right occipital cortex (left visual field) is prevented from reaching the left angulate gyrus.

> *NB:* It is therefore mandatory to examine reading ability in the context of a right hemianopia.

Agnosia

Lesions of the inferior occipitotemporal area may produce a wide range of clinical features. Bilateral disease may produce visual agnosia—the inability to recognize objects by sight—while the ability to recognize by touch is retained. Prosopagnosia implies the inability to recognize and distinguish between faces. Colour vision too has its seat in this area, each half of the visual field being represented contralaterally. Lesions here may therefore also result in contralateral (cerebral) hemi-achromatopsia with total loss or relative desaturation of colour.

Visual hallucinations

Significant visual impairment due to pathology anywhere along the visual pathway, from the eye to the primary visual cortex, may result in the emergence of complex visual hallucinations. This condition (Charles Bonnet syndrome) is thought to represent a release phenomenon, secondary to deafferentation of the visual association areas, which then exhibit spontaneous activity, with resultant complex (formed) visual hallucinations. Such hallucinations are often brilliantly clear and detailed, in contrast to the patient's normally indistinct vision, and are recognized by the patient as unreal, often after initial deception. Hallucinatory content is usually pleasant but may be distressing. Patients aware of the unreality of their visions often do not admit their existence for fear of being labelled insane. Sensitive history taking and reassurance are usually sufficient.

Migraine

Clinical features

Migraine is an often familial disorder, more common in females, characterized by recurrent attacks of headache widely variable in intensity, duration and frequency. The headache is commonly unilateral, associated with nausea and vomiting, and may be preceded by or associated with neurological and mood disturbances. However, all these characteristics are not necessarily present during each attack or in every patient. The main types of migraine are as follows.

Common migraine

Common migraine (migraine without aura) is characterized by headache with autonomic nervous system dysfunction (e.g. pallor and nausea), but without stereotypical neurological or ophthalmic features as in classical migraine (*see* later).

- Premonitory features include changes in mood, frequent yawning or other non-specific prodromal symptoms such as poor concentration.
- The headache starts anywhere on the cranium and is pounding or throbbing. It usually spreads to involve one

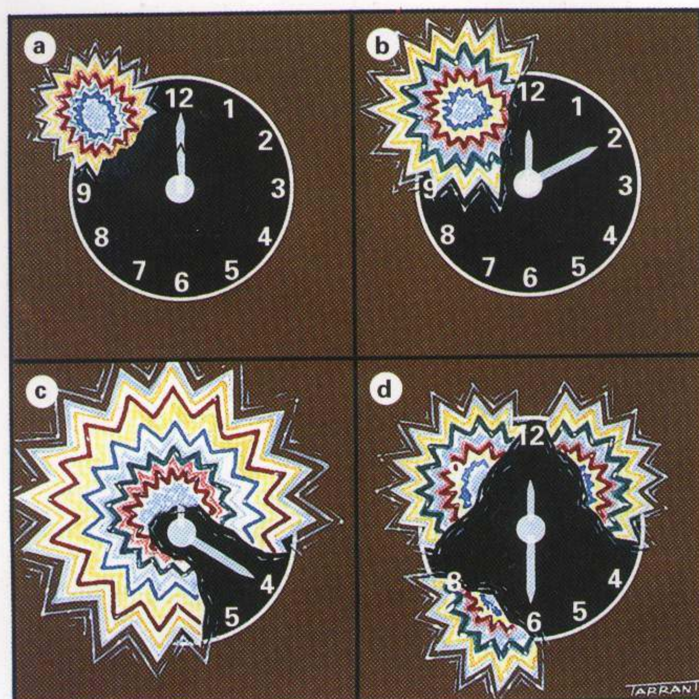


Fig. 18.108
Progression of classic migrainous fortification spectrum and scintillating scotoma

half or even the whole head. If retro-orbital, the pain may be mistaken for ocular or sinus disease.

- During the attack, which lasts from hours to a day or more, the patient is frequently photophobic and phonophobic and seeks relief in a quiet, dark environment or through sleep.
- Because of the absence of the well-known migrainous visual distortions, severe nausea and vomiting, common migraine often goes unrecognized.

Classical migraine

Classical migraine (migraine with aura) is less common but better recognized (Fig. 18.108).

- The attack is heralded by a visual aura which lasts about 20 minutes. This may consist of bright or dark spots, zig-zags, heat haze distortions, jig-saw puzzle effects, scintillating scotomata, tunnel vision or fortification spectra, which may progress to homonymous hemianopia.
- A small bright positive paracentral scotoma develops, lined on one side with luminous zig-zag lines.
- After several minutes the fortification spectrum gradually enlarges with the open end pointing centrally. It is often lined on the inner edge by an absent area of vision (negative scotoma).
- As the scotoma expands it may drift towards the temporal periphery before breaking up.

> ***NB:*** These visual features, supposedly pathognomonic of migraine, may rarely be caused by degenerative arterial disease in the occipital poles.

- The headache follows the aura and is usually hemicranial, opposite the hemianopia and is accompanied by nausea and photophobia. It may, however, be absent, trivial or very severe, with considerable variation between attacks even in the same individual.

Cluster headache

Cluster headache (migrainous neuralgia) is a migraine variant which typically affects men during the fourth and fifth decades of life. It is of particular interest to ophthalmologists because it is associated with ocular features and may initially be misdiagnosed as an ocular problem. The condition is characterized by a stereotyped headache accompanied by various autonomic phenomena occurring almost every day for a period of some weeks.

- The headache is unilateral, oculotemporal, excruciating, sharp and deep.
- It begins relatively abruptly, lasts between 10 minutes and 2 hours, and then clears quickly.
- It may occur several times in a 24-hour period, often at particular times, not infrequently at around 2 a.m.
- Once the 'cluster' is over, there may be a long headache-free interval of several years.
- Associated autonomic phenomena include lacrimation, conjunctival injection and rhinorrhoea.

> ***NB:*** Cluster headaches are also a common cause of a transient or permanent postganglionic Horner syndrome.

Other types of migraine

1. **Focal migraine** is characterized by transient dysphasia, hemisensory symptoms or even focal weakness in addition to other symptoms of migraine.
2. **Migraine sine migraine** is characterized by episodic visual disturbances without headache. Elderly patients with a past history of classical migraine are typically affected.
3. **Retinal migraine** is characterized by acute, transient, unilateral loss of vision. Since this may occur in middle-aged patients without past history of migraine, it is prudent to investigate such individuals as undergoing attacks of retinal embolization, until proved otherwise.
4. **Ophthalmoplegic migraine** is rare and typically starts before the age of 10 years. It is characterized by a recurrent transient third nerve palsy which begins after the headache.
5. **Familial hemiplegic migraine** is characterized by a failure of full recovery of focal neurological features after an attack of migraine subsides.
6. **Basilar migraine** occurs in children. It is characterized by a typical migrainous aura associated with numbness and tingling of the lips and extremities which is often bilateral. Ataxia of gait and speech also occur, with occasional impairment of consciousness.

Management

1. **General measures** include the elimination of conditions and agents that may precipitate an attack of migraine, such as coffee, chocolate, alcohol, cheese, oral contraceptives, stress, lack of sleep and long intervals without food.
2. **Prophylaxis** is indicated if the frequency and/or severity of the attacks are beyond the patient's tolerance. This may involve beta-adrenergic blockers, calcium channel blockers, amitriptyline, clonidine, pizotifen and low-dose aspirin.
3. **Treatment** of an acute attack may be with simple analgesics (aspirin, codeine analogues, paracetamol or a NSAID) and, if appropriate, an anti-emetic such as metoclopramide. Other drugs, usually reserved for patients refractory to analgesics, include sumatriptan and ergotamine tartrate.

Differential diagnosis

Visual phenomena

The visual phenomena of migraine are typically binocular, zig-zag, scintillating and migrate within the visual field. This is often followed by a scotoma and/or homonymous visual loss. The patient may report loss of vision in the eye ipsilateral to the hemianopia. The following conditions should be considered in the differential diagnosis:

1. **Acute posterior vitreous detachment** is characterized by photopsia, usually associated with the sudden onset of floaters. The flashing lights are usually projected into the temporal visual field and may be precipitated by movements of the head or eyes.
2. **Transient ischaemic attacks** due to retinal microembolization are unilateral and not scintillating. The patient often describes a 'shade' or 'cloud' which typically starts in the upper or lower parts of the visual field and spreads centrally. It lasts several minutes and clears from the centre to the periphery.
3. **Transient visual obscurations** last only a few seconds and are characterized by a 'greying out' or 'darkening' of vision in one or both eyes. They classically occur in patients with papilloedema and are often precipitated by changes in posture. They may also precede anterior ischaemic optic neuropathy in patients with giant cell arteritis.

Neuralgias

The following conditions should be considered in the differential diagnosis of ocular or periocular pain in the absence of apparent physical disease:

1. **Herpes zoster ophthalmicus** frequently presents with pain 2–3 days before the onset of the characteristic vesicular rash.
2. **Trigeminal neuralgia** is characterized by brief attacks of severe pain that start in the distribution of one of the divisions of the trigeminal nerve. The pain is paroxysmal and sharp, like an electric shock, usually occurring in multiple bursts lasting a few seconds, in rapid succession. Facial sensation is normal. Treatment involves anti-epileptic drugs such as carbamazepine, phenytoin and sodium valporate. Trigeminal neuralgia of compressive aetiology may necessitate intracranial surgical decompression of the trigeminal nerve.
3. **Raeder paratrigeminal neuralgia** occurs in middle-aged men. It is characterized by severe unilateral headache with periocular pain in the distribution of the first division of the trigeminal nerve associated with an ipsilateral Horner syndrome. The pain may last from hours to weeks before it resolves spontaneously.
4. **Greater occipital neuralgia** is characterized by attacks of pain that begin in the occipital region and then spread to the eye, temple and face. The attacks frequently occur at night and are associated with flushing of the face, dizziness and sometimes ipsilateral nasal obstruction. Examination during an attack may reveal extreme tenderness between the mastoid process and occipital protuberance.
5. **Ophthalmodynia periodica** is characterized by short, sharp stabbing ocular pain which often causes the patient to place the hand over the involved eye. A second series of episodes may immediately follow the initial attack.
6. **Ice-pick syndrome** is characterized by attacks of momentary, multifocal, sharp pain around the skull, face and eyes. Unlike trigeminal neuralgia there are no specific trigger points; the pain also does not conform to the anatomical distribution of the trigeminal nerve. Facial pain in a young person may occasionally be a manifestation of multiple sclerosis.

Intracranial aneurysms

Applied anatomy

The arterial supply to the brain comes from the internal carotid and vertebral arteries.

1. **The vertebral** arteries enter the cranial cavity through the foramen magnum and unite into the basilar artery, which ascends on the ventral surface of the brain stem. After giving rise to branches to the brain stem, the basilar artery divides into its terminal branches: the posterior cerebral arteries.
2. **The internal carotid** arteries enter the base of the skull through the carotid canal and the cranial cavity through the foramen lacerum, at the apex of the petrous part of the temporal bone. They then run forwards in the cavernous sinus, lateral to the pituitary gland before ascending, lateral to the optic chiasm and dividing into the anterior and middle cerebral arteries.
3. **The circle of Willis**. The anterior cerebral arteries are connected by the anterior communicating artery. The middle and posterior cerebral arteries are connected by the posterior communicating artery (Fig. 18.109). This anastomosis forms the circle of Willis, which lies in the subarachnoid space on the ventral surface of the brain.

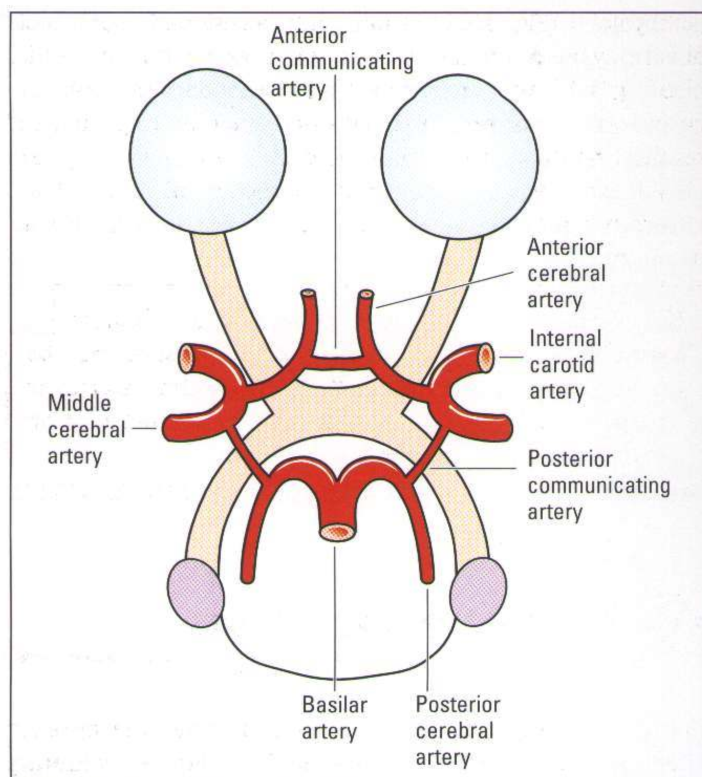


Fig. 18.109
Dorsal view of the circle of Willis (Courtesy of G. Robertson)

Neurological considerations

Intracranial aneurysms are saccular arterial outpouchings that most commonly develop at the branching points of the major arteries coursing through the subarachnoid space at the base of the brain. Eighty-five per cent arise from the anterior half of the circle of Willis. Their prevalence ranges from 1% to 6% among adults in large autopsy series. Aneurysms are multiple (usually two or three) in about 25% of cases. The majority of aneurysms remain asymptomatic during life.

Complications

1. **Subarachnoid haemorrhage** due to rupture is by far the most frequent complication. This life-threatening event presents with sudden onset of severe headache, photophobia, clouding consciousness, vomiting and signs of meningeal irritation, including neck stiffness and positive Kernig sign. Blood-stained CSF is revealed on lumbar puncture. Approximately 12% of patients die before receiving medical attention, 40% of hospitalized patients die within 1 month and more than one-third of those that survive suffer major neurological deficits.
2. **Pressure effects** are less frequent and associated with 'giant' aneurysms (larger than 25 mm). The most common symptom is headache; associated signs depend on the location of the lesion and are frequently neuro-ophthalmological, such as third nerve palsy from aneurysm of the posterior communicating artery. Such 'giant' aneurysms also have a high subsequent rupture rate with an estimated frequency of 6% per year. The interval between warning mass signs and rupture varies from 1 day to 4 months, so that early diagnosis is paramount.



Fig. 18.110
Arteriogram with subtraction showing a small posterior communicating aneurysm (arrow) (Courtesy of S. Cudlip)

Neuroimaging

MRI (*see* Fig. 18.9), MRA or conventional (intra-arterial) angiography (Fig. 18.110) are useful in diagnosis. While the first two are capable of demonstrating large to medium-sized aneurysms, they often fail to detect those smaller than 5 mm. Despite infrequent but potentially serious risks including vascular damage and permanent neurological deficits, conventional angiography is still the 'gold standard', particularly prior to surgical intervention.

Treatment

Definitive treatment is surgical, aimed at excluding the aneurysmal sac from the intracranial circulation while preserving the parent artery. This involves placing a clip around the neck of the aneurysm or less frequently the insertion of soft metallic coils within the lumen of the aneurysm.

Neuro-ophthalmic aspects

Ocular motor nerve palsies

1. **Isolated third nerve palsy** may be caused by compression by an aneurysm of the posterior communicating artery at its junction with the internal carotid artery in the subarachnoid space (*see* Fig. 18.77). Presentation is typically with ipsilateral frontal headache and a total third nerve palsy (with internal ophthalmoplegia).

> *NB:* Pupil sparing in a total third nerve palsy almost always excludes an aneurysm. Pain is rarely absent; however, its absence does not exclude an aneurysm.

2. **Isolated sixth nerve palsy** can occur with aneurysms of the intracavernous part of the internal carotid artery, but very rarely from involvement in the subarachnoid space.

3. **Combined palsies** of the third and sixth nerves occur with intracavernous carotid aneurysms, although this may also occur in other cavernous sinus lesions. The fourth nerve may also be involved but this is frequently obscured by the other lesions. Although parasympathetic innervation is commonly damaged, mydriasis may not occur; the pupil may even be miosed because of coexistent damage to the sympathetic fibres.

> *NB:* An important sign of cavernous sinus lesions is sensory loss over the distribution of the first division of the trigeminal nerve.

Visual loss

1. **Monocular** visual loss is most frequently caused by compression of the intracranial part of the optic nerve by aneurysms arising from the internal carotid artery near the origin of the ophthalmic artery, at its terminal bifurcation (*see* Fig. 18.93). The clinical picture is that of unilateral acute or progressive visual loss occasionally associated with orbital pain, which may initially be misdiagnosed as retrobulbar neuritis.
2. **Visual field defects** involving the nasal field may be caused by a giant aneurysm at or near the origin of the ophthalmic artery. Rarely, a giant aneurysm may compress the lateral aspect of the chiasm and cause a nasal field defect which is initially unilateral but may become bilateral if the chiasm is pushed across against the opposite carotid artery. Homonymous defects and cortical blindness may be caused by transient or permanent ischaemia of the retrochiasmal visual pathways.

> *NB:* Carotid aneurysms may also invade the sella and mimic pituitary adenomas.

Terson syndrome

Terson syndrome refers to the combination of intraocular haemorrhage and subarachnoid haemorrhage due to aneurysmal rupture, most commonly arising from the anterior communicating artery. However, intraocular haemorrhage may also occur with subdural haematoma and acute elevation of intracranial pressure from other causes. The haemorrhage is frequently bilateral, and typically intraretinal or preretinal (subhyaloid) (Fig. 18.111) although occasionally subhyaloid blood may break into the vitreous. It is probable that intraocular bleeding is due to retinal venous stasis secondary to increase in cavernous sinus pressure. Vitreous haemorrhage usually resolves spontaneously within a few months and the long-term visual prognosis is good in the majority of cases. Early vitrectomy may be considered for dense bilateral vitreous involvement.

> *NB:* Papilloedema may be a feature of subarachnoid haemorrhage. Elevation of intracranial pressure may be caused by blockage of CSF flow within the ventricular system (obstructive hydrocephalus) or defective CSF absorption by the arachnoid villi.

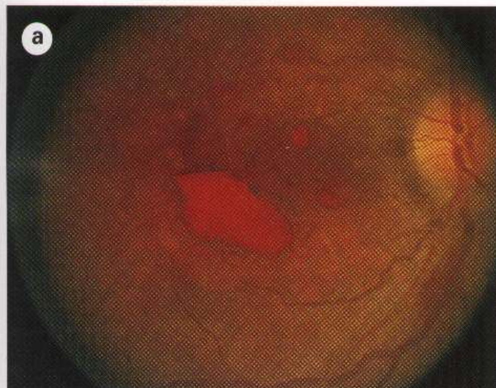
Myasthenia gravis

Myasthenia gravis is an uncommon autoimmune disorder, characterized by weakness and fatiguability of voluntary musculature. The condition affects females twice as commonly as males. Diagnostic tests include the edrophonium test, serum acetylcholine receptor antibody levels and electromyography. Myasthenia gravis may be (a) *ocular*, (b) *bulbar* or (c) *generalized* (*see* Chapter 20).

Ocular features

Ocular involvement occurs in 90% of cases and is the presenting feature in 60%. It is characterized by the following:

1. **Ptosis** is insidious, bilateral and frequently asymmetrical.
   - It is worse at the end of the day and least on awakening.
   - Ptosis is worse on prolonged upgaze due to fatigue.
   - If one eyelid is elevated manually as the patient looks up, the fellow eyelid will show fine oscillatory movements.
   - Cogan twitch sign is a brief upshoot of the eyelid as the eyes saccade from depression to the primary position.
   - Positive ice test: the degree of ptosis improves after an ice pack is placed on the eyelid for 2 minutes. The test is negative in non-myasthenic ptosis.
2. **Diplopia** is frequently vertical, although any or all of the extraocular muscles may be affected. A pseudo-



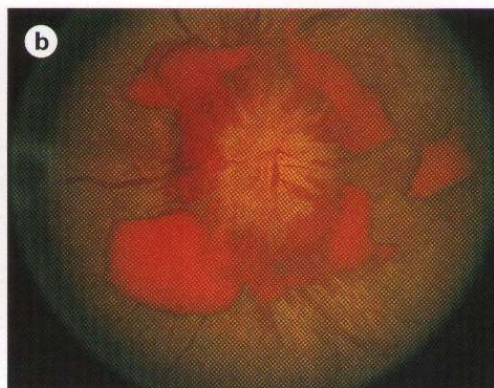


Fig. 18.111
Terson syndrome. (**a**) Intraretinal haemorrhages and a large subhyaloid haemorrhage; (**b**) oedematous optic disc surrounded by subhyaloid haemorrhages (Courtesy of Wilmer Institute)

internuclear ophthalmoplegia may be seen. Patients with stable deviations may benefit from muscle surgery, botulinum toxin injection or a combination of both.

3. **Nystagmoid movements** may be present on extremes of gaze.

Edrophonium test

Edrophonium is a short-acting anticholinesterase which increases the amount of acetylcholine available at the neuromuscular junction. In myasthenia this results in transient improvement of symptoms and signs such as weakness, ptosis and diplopia. The estimated sensitivity is 85% in ocular and 95% in systemic myasthenia. Potential but uncommon complications include bradycardia, loss of consciousness and even death. The test should therefore never be performed without an assistant, and a resuscitation trolley should also be close at hand in case of sudden cardiorespiratory arrest. The test is performed as follows:

1. Objective baseline measurements are made of the ptosis or diplopia with a Hess test (*see* Chapter 16).
2. Intravenous injection of atropine 0.3 mg is given to minimize muscarinic side effects.
3. Intravenous test dose of 0.2 ml (2 mg) edrophonium hydrochloride is given. If definite symptomatic improvement is noted the test is terminated forthwith.
4. The remaining 0.8 ml (8 mg) is given after 60 seconds, provided there is no hypersensitivity.
5. Final measurements/repeat Hess testing are made and the results compared, remembering that the effect lasts only 5 minutes (Fig. 18.112).

Chronic progressive external ophthalmoplegia

Chronic progressive external ophthalmoplegia (CPEO) refers to a group of disorders characterized by the triad of ptosis, slowly progressive bilateral ocular immobility and ragged-red fibre myopathy (Fig. 18.113d).

Classification

1. **Isolated** presents in adult life and is the mildest.
2. **Oculopharyngeal dystrophy** is of intermediate severity and presents in adolescence or early childhood. It is characterized by weakness of the pharyngeal muscles and wasting of the temporalis.
3. **Kearns–Sayre syndrome**, the most severe, presents in childhood and is associated with pigmentary retinopathy (Fig. 18.113c) and heart block (*see* Chapter 20).

Clinical features

1. **Ptosis**, usually the first sign, is bilateral and asymmetrical (Fig. 18.113a). Surgical correction may improve compensatory head posture but does not restore normal movements and is associated with a risk of corneal exposure.
2. **External ophthalmoplegia** begins in young adulthood and typically is symmetrical. It is characterized by a progressive course without remission or exacerbation. Initially upgaze is involved (Fig. 18.113b); subsequently lateral gaze is affected so that the eyes may become virtually fixed. A minority of patients with diplopia may benefit from surgery.

Essential blepharospasm

Clinical features

Essential blepharospasm is an uncommon but distressing idiopathic disorder which presents in the sixth decade and affects women more commonly than men by a 3:1 ratio. It is characterized by progressive involuntary spasm of the orbicularis oculi and upper facial muscles. In severe cases blepharospasm is disabling because it may temporarily render the patient functionally blind (Fig. 18.114a). Spasms may be precipitated by reading, driving, stress or bright light, and alleviated by talking, walking and relaxation.





Fig. 18.112
Positive edrophonium test in myasthenic ptosis. **(a)** Prior to injection; **(b)** 2 minutes after injection



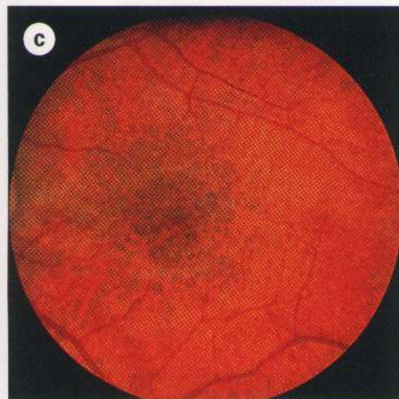
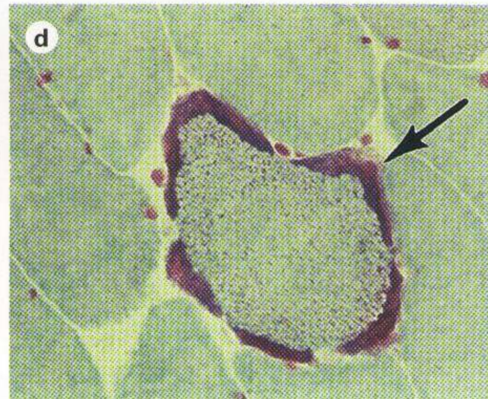



Fig. 18.113
Kearns–Sayre syndrome. (**a**) Symmetrical ptosis; (**b**) ophthalmoplegia; (**c**) pigmentary retinopathy; (**d**) histology showing ragged-red muscle fibre (arrow) (Courtesy of Wilmer Institute)




Fig. 18.114
Essential blepharospasm. (**a**) During attack; (**b**) after attack

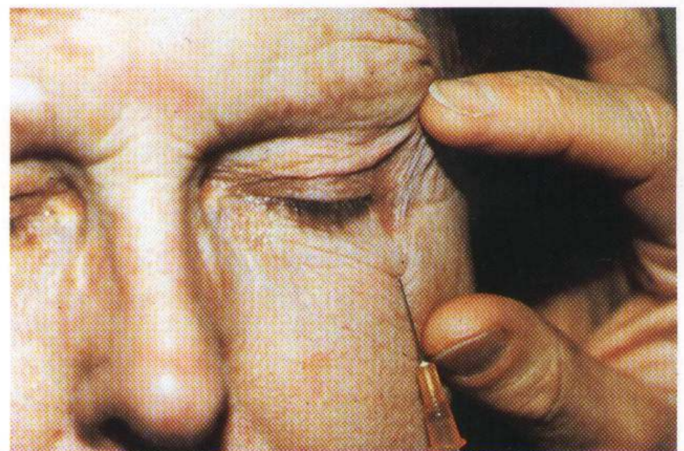


Fig. 18.115
Botulinum toxin injection for essential blepharospasm

1. **Meige syndrome** is a combination of blepharospasm and involvement of the lower facial and neck muscles.
2. **Breughel syndrome** is associated with severe mandibular and cervical muscle involvement.

Treatment

Prior to commencing treatment it is important to exclude reflex blepharospasm, most commonly due to ocular surface disease such as filamentary keratitis.

1. **Medical** treatment with a great variety of drugs has been reported to ameliorate specific types of blepharospasm, but their efficacy is disappointing.
2. **Botulinum toxin** injected along the upper and lower eyelid and eyebrow affords temporary relief in most patients (Fig. 18.115). By interference with acetylcholine release from nerve terminals it results in temporary paralysis of the injected muscles. Most patients require repeat injections every 3–4 months; progressively larger doses may be needed. Side effects include lagophthalmos and ectropion or entropion, depending on the tone of the eyelids before the injection. Accidental migration of the toxin into the orbit may result in ptosis and diplopia due to paralysis of the levator or extraocular muscles.
3. **Surgical** treatment involves removal of the entire orbicularis, corrugator and procerus muscles. Such radical surgery is reserved for patients who cannot tolerate or are unresponsive to botulinum toxin.

Neurofibromatosis

Neurofibromatosis is a hereditary disorder that primarily affects cell growth of neural tissues. Inheritance is AD with irregular penetrance and variable expressivity. The mutation rate is high. The two main types are: (a) *type 1 (NF-1)* and (b) *type 2 (NF-2)*.

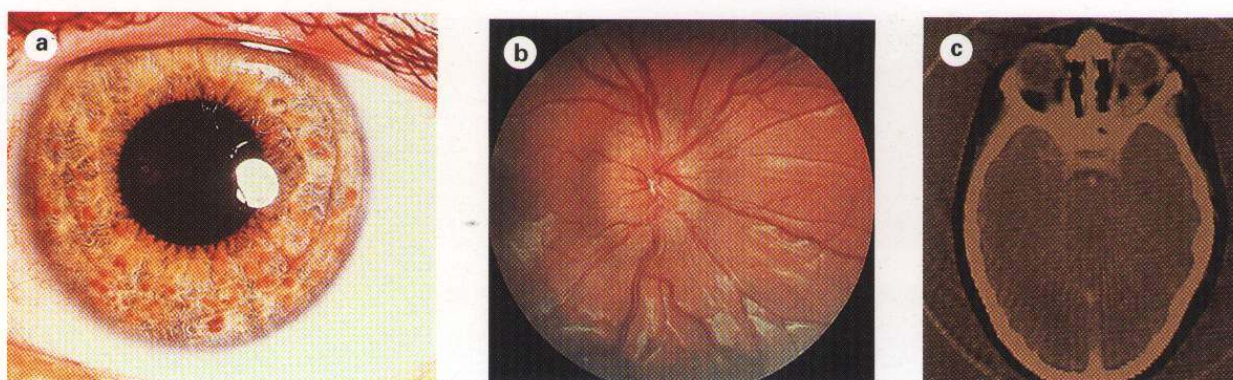


Fig. 18.116
NF-1. (**a**) Lisch nodules; (**b**) disc oedema due to optic nerve glioma; (**c**) CT scan showing optic nerve glioma (Courtesy of Wilmer Institute)

NF-1

NF-1 is the most common phakomatosis, affecting 1:4000 individuals, and it presents in childhood. The gene locus is on 17q11. The systemic features are discussed in Chapter 20. The ocular features are as follows:

1. **Orbital involvement** may be caused by one of the following:
   a. *Optic nerve glioma* (Fig. 18.116b and c) develops in about 15% of patients. It may be unilateral or bilateral and tends to extend posteriorly to involve the chiasm and hypothalamus (*see* Fig. 17.66).
   b. *Other neural tumours* including neurilemmoma, plexiform neurofibroma and meningioma.
   c. *Spheno-orbital encephalocele* is caused by absence of the greater wing of the sphenoid bone (Fig. 18.117). It characteristically causes a pulsating proptosis, unassociated with either a bruit or a thrill.
2. **Eyelid neurofibromas**, which may be either nodular (Fig. 18.118) or plexiform (Fig. 18.119), tend to develop early in life. When involving the upper lid, they frequently cause a mechanical ptosis.
3. **Iris lesions**
   a. *Lisch nodules* develop during the second to third decades and are eventually present in 95% of cases (*see* Fig. 18.116a).
   b. *Congenital ectropion uveae* is uncommon and may be associated with glaucoma (*see* Fig. 9.138).
   c. *Mammillations* are rare (*see* Fig. 4.81).
4. **Prominent corneal nerves** may occur (Fig. 18.120).
5. **Glaucoma** is relatively rare and, when present, is usually unilateral and congenital. About 50% of patients with glaucoma manifest ipsilateral neurofibroma of the upper eyelid and facial hemiatrophy. The mechanisms responsible for the pressure rise are discussed in Chapter 9.

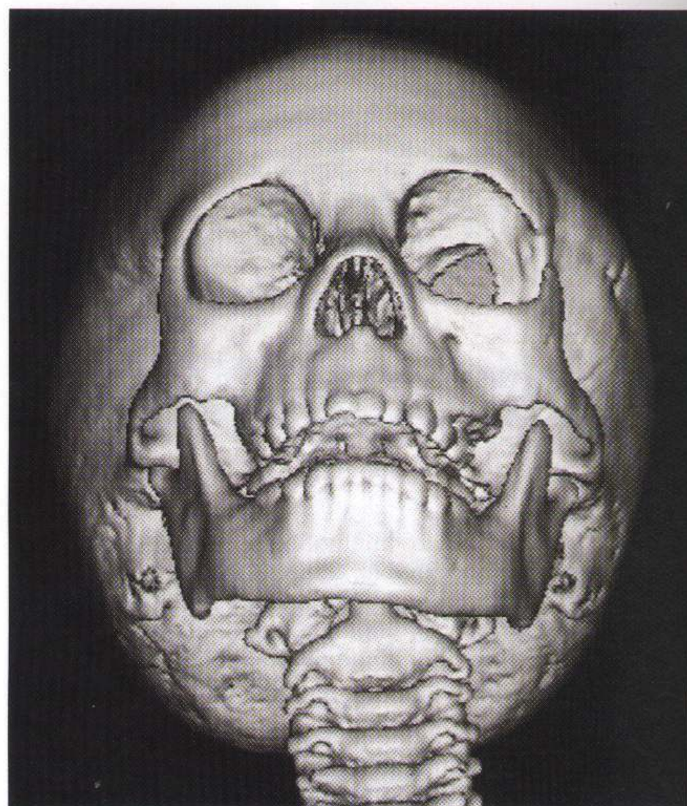


Fig. 18.117
Three-dimensional CT scan showing absence of the left greater wing of the sphenoid in NF-1 (Courtesy of D. Armstrong)

6. **Fundus lesions**
   a. *Choroidal naevi*, which may be multifocal and bilateral, are common. Patients with NF-1 and naevi are at increased risk for the subsequent development of choroidal melanoma.
   b. *Retinal astrocytomas*, identical to those in tuberous sclerosis, are rare.


Fig. 18.118
Nodular neurofibroma

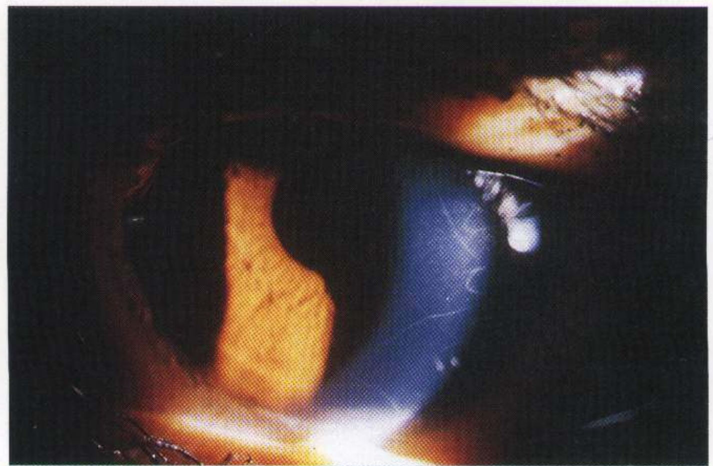

Fig. 18.120
Prominent corneal nerves


Fig. 18.119
Plexiform neurofibroma (Courtesy of K. Nischal)

NF-2

NF-2 is much less common than NF-1 and affects 1 in 40,000 individuals. The responsible gene locus is on 22q12. The main manifestations are bilateral acoustic neuromas and other CNS tumours (*see* Chapter 20). The following ocular lesions are often the first signs of the disease and may therefore assist in presymptomatic diagnosis:

1. **Cataract** affects about two-thirds of patients. The opacities develop prior to the age of 30 years and may be posterior subcapsular or capsular, cortical or mixed.
2. **Fundus lesions** consisting of combined hamartomas of the retinal pigment epithelium and retina and perifoveal epiretinal membranes are relatively common.
3. **Ocular motor defects** are present in about 10% of cases.
4. **Less common** findings include optic nerve sheath meningioma, optic nerve glioma, unilateral Lisch nodules, and an abnormal electroretinogram.